

### Question 1 of 206

A patient with end stage renal disease is receiving haemodialysis and erythropoietin.

Which of the following does erythropoietin therapy cause?

(Please select 1 option)

<input type="radio"/>	Hypotension
<input type="radio"/>	Idiopathic intracranial hypertension
<input type="radio"/>	Myositis
<input type="radio"/>	Osteoporosis
<input type="radio"/>	Seizures

<input checked="" type="radio"/>	Seizures <b>Correct</b>
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Hypertension is a frequent problem associated with [erythropoietin](#) and may induce seizures.

A particular symptom is the onset of sudden stabbing migraine-like headache and should raise awareness to the possibility of hypertensive crisis.

Other adverse effects of treatment with erythropoietin include:

- Hyperkalaemia in uraemic patients
- Increased PCV (especially with misuse by normal individuals)
- Thrombocythaemia
- Shunt thrombosis
- Induction of iron deficiency
- Skin rashes
- Urticaria, and
- Flu-like illness.

## Question 2 of 206

A 56-year-old female presents at the general practitioner with weakness.

A full blood count (FBC) reveals a haemoglobin concentration of 105 g/L (115-165) and a mean cell volume (MCV) of 104 fL (80-96), but no other abnormality.

Which of the following may account for this?

(Please select 1 option)

<input type="radio"/>	Hormone replacement therapy (HRT)
<input type="radio"/>	Scurvy
<input type="radio"/>	Thyrotoxicosis
<input type="radio"/>	Ulcerative colitis
<input type="radio"/>	Zollinger-Ellison syndrome

<input checked="" type="radio"/>	Scurvy <b>Correct</b>
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This is a tricky question. However, if you bear in mind this patient's symptoms and her FBC you should come to the correct conclusion.

She has weakness and in association with a mild anaemia and her increased MCV a vitamin C deficiency is most probable. Anaemia of this level should not cause weakness in itself.

Scurvy should not be thought of as a disease of the past, as cases continue to be diagnosed in children and adults. Clinical manifestations vary, and can be seen within 8-12 weeks of irregular or inadequate dietary intake. The early stages are characterised by malaise, fatigue and lethargy.

Dehydroascorbic acid, the oxidative product of ascorbic acid metabolism, passively penetrates cellular membranes and is the preferred form for erythrocytes and leukocytes.

Ascorbic acid is a reversible biologic reductant, and provides reducing equivalents for a number of biochemical reactions involving iron and copper.

Because of this property, it functions as a cofactor, enzyme complement, co-substrate, or a strong antioxidant in a variety of reactions and metabolic processes. Ascorbic acid provides electrons needed to reduce molecular oxygen. These anti-oxidant capabilities also stabilize a number of other compounds, including vitamin E and folic acid. It is a cofactor for reduction of folate to dihydro-and-tetrahydrofolate.

Therefore macrocytic anaemia in scurvy may occur due to two reasons: oxidative hemolysis and folate metabolism defects.

Continued deficiency leads to:

- Anaemia
- Myalgia
- Bone pain
- Bruising
- Petechial and perifollicular haemorrhages
- Corkscrew hairs
- Gum disease
- Poor wound healing, and
- Mood changes.

Late stages can lead to:

- Generalised oedema
- Severe jaundice
- Haemolysis
- Haemorrhage
- Neuropathy
- Convulsions, and
- Death.

Treatment for scurvy is vitamin C supplementation, and recovery is usually complete within three months.

HRT can affect folate storage and absorption, but not usually to an extent to cause these biochemical changes. Ulcerative colitis is more likely to be associated with iron (Fe) deficiency anaemia as is Zollinger-Ellison syndrome and ulcerative colitis are both associated with iron-deficiency anaemia, and therefore a microcytosis.

Hypothyroidism, not thyrotoxicosis, is associated with macrocytosis.

### **Question 3 of 206**

Which of the following is true with regard to anti-neutrophilic cytoplasmic autoantibodies?

(Please select 1 option)

<input type="radio"/>	ANCA positive glomerulonephritis characteristically causes nephrotic syndrome
<input type="radio"/>	They are increased in systemic lupus erythematosus (SLE)
<input type="radio"/>	They are positive only in Wegener's syndrome associated with renal disease I
<input type="radio"/>	They are present in inflammatory bowel disease
<input type="radio"/>	They cause neutropenia in SLE
<input checked="" type="radio"/>	They are present in inflammatory bowel disease <b>This is the correct answer</b>

Eighty-five percent of untreated subjects with Wegener's will have circulating anti-neutrophil cytoplasmic antibody (cANCA) and those with limited disease are less likely to have positive serology.

Perinuclear anti-neutrophil cytoplasmic antibody (pANCA) is present in approximately 70% with ulcerative colitis and less than 20% of Crohn's patients.

Neither p nor c-ANCA is typical of SLE.

Initial renal damage causes proteinuria (focal proliferative glomerulonephritis) but renal function can deteriorate rapidly with development of acute focal necrotising glomerulonephritis.

#### Question 4 of 206

A 20-year-old Caucasian student returns from Ghana with a spiking temperature and nocturnal sweats. She has 0.5% of red blood cells infected with *Plasmodium falciparum*.

Which of the following is correct, as it relates to quinine therapy in this case?

(Please select 1 option)

<input type="radio"/>	Glucose levels should be monitored in those being treated with quinine
<input type="radio"/>	Pregnancy is a contraindication for quinine
<input type="radio"/>	Quinine is contraindicated in those taking mefloquine prophylactically
<input type="radio"/>	Quinine must always be given parenterally initially
<input type="radio"/>	The dose of quinine should be reduced in liver impairment

<input checked="" type="radio"/>	Glucose levels should be monitored in those being treated with quinine <b>Correct</b>
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Severe malaria is indicated by more than 1% of RBC infected.

Hypoglycaemia is an important side effect of quinine therapy and should be monitored in those having intravenous quinine.

Intravenous infusion of quinine is reserved for severe or cerebral malaria (most deaths from *M. falciparum* occur in first 96 hours of starting treatment).

The initial dose should NOT be reduced in those severely ill with renal/hepatic impairment.

High doses of quinine in pregnancy are teratogenic in the first trimester. However, in malaria, the benefit of treatment outweighs the risk. [WHO Guidelines \(2006\)](#) recommend artemisinins are the first line in the second and third trimester. In the first trimester, both artesunate and quinine are considered treatment options. In severe malaria, any available treatment should be started without delay as both the mother and foetus' life are in danger.

### Question 5 of 206

By which of the following can folic acid metabolism be affected?

(Please select 1 option)

<input type="radio"/>	Ibuprofen
<input type="radio"/>	Penicillin
<input type="radio"/>	Pyrimethamine
<input type="radio"/>	Tetracycline
<input type="radio"/>	Vitamin B12

<input checked="" type="radio"/>	Pyrimethamine This is the correct answer
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Drugs which inhibit dihydrofolate reductase are:

- methotrexate
- pyrimethamine, and
- trimethoprim.

Drugs which interfere with absorption/storage of folate are:

- phenytoin
- primidone, and
- oral contraceptives.

### Question 6 of 206

Heinz bodies in red blood cells in haemolytic anaemia are present in which of the following?

(Please select 1 option)

<input type="radio"/>	<i>Clostridium welchii</i> septicaemia
<input type="radio"/>	Cold agglutinin disease

<input type="radio"/>	Glucose 6 phosphate dehydrogenase deficiency
<input type="radio"/>	Paroxysmal nocturnal haemoglobinuria
<input type="radio"/>	Post splenectomy

<input checked="" type="radio"/>	Glucose 6 phosphate dehydrogenase deficiency <b>This is the correct answer</b>
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Heinz bodies are oxidised denatured haemoglobin.

Post-splenectomy causes:

- target cells
- pappenheimer bodies (siderotic granules), and
- Howell-Jolly bodies (DNA remnants).

### Question 7 of 206

A previously fit 30-year-old male presents with a two-month history of weight loss, tiredness and nausea.

Investigations show:

<b>Haemoglobin</b>	105 g/L	(130-180)
<b>MCV</b>	88 fL	(80-96)
<b>White cell count</b>	$6.0 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$450 \times 10^9/\text{L}$	(150-400)
<b>Serum sodium</b>	130 mmol/L	(137-144)

<b>Serum potassium</b>	5.7 mmol/L	(3.5-4.9)
<b>Serum urea</b>	3.0 mmol/L	(2.5-7.5)
<b>Serum creatinine</b>	78 µmol/L	(60-110)
<b>Serum total T4</b>	55 nmol/L	(50-150)
<b>Serum TSH</b>	8 mU/L	(0.4-5)

Which of the following is the most useful diagnostic investigation?

(Please select 1 option)

<input type="radio"/>	Anti-thyroid peroxidase antibody titre
<input type="radio"/>	Free thyroxine concentration
<input type="radio"/>	Insulin tolerance test
<input type="radio"/>	Short Synacthen test
<input type="radio"/>	TRH test
<input checked="" type="radio"/>	Short Synacthen test <b>This is the correct answer</b>

This patient presents with weight loss, tiredness, and nausea. He has hyponatraemia, hyperkalaemia, and what appears to be a mild primary hypothyroidism.

The diagnosis is likely to be Addison's (primary hypoadrenalism) disease and the most appropriate test would be a short Synacthen test.

The link between Addison's and primary hypothyroidism is that they are both conditions in the complex of autoimmune polyendocrine syndrome. Other possible associations of this cluster would be:

- type 1 diabetes
- vitiligo
- pernicious anaemia, and
- chronic active hepatitis.

An insulin tolerance test is contraindicated in patients in whom cortisol is less than 100 nmol/L.

A thyrotropin-releasing hormone (TRH) test is rarely performed these days and really is an irrelevance.

### Question 8 of 206

A 26-year-old woman presented at 35 weeks of pregnancy with profuse vaginal bleeding. She had suffered two previous miscarriages.

She had a pulse of 95 beats per minute, blood pressure of 110/84 mmHg, and no fetal heart sounds were audible.

Investigations revealed:

<b>Haemoglobin</b>	98 g/L	(115 - 165)
<b>Platelets</b>	$66 \times 10^9/\text{L}$	(150 - 400)
<b>Prothrombin time</b>	21 sec	(11.5- 15.5)
<b>APTT</b>	52 sec	(30-40)

<b>Fibrinogen</b>	0.5 g/L	(2-4)
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Which is the most appropriate next step in management?

(Please select 1 option)

<input type="radio"/>	Antithrombin III infusion
<input type="radio"/>	Fibrinogen replacement infusion (cryoprecipitate)
<input type="radio"/>	Intravenous heparin
<input type="radio"/>	Platelet transfusion
<input type="radio"/>	Transfusion of two units group O rhesus D negative blood
<input checked="" type="radio"/>	Fibrinogen replacement infusion (cryoprecipitate) <b>This is the correct answer</b>

The clinical picture is disseminated intravascular coagulation.

When bleeding is the major problem, the aim is to maintain the prothrombin and activated thromboplastin time at a ratio of 1.5 times of the control and the fibrinogen level above 1 g/L.

Platelet transfusion is recommended if the count is less than  $50 \times 10^9/L$ .

Anaemia is not very severe so in this case, fibrinogen replacement would be the appropriate first choice with blood transfusion an addition if bleeding continues and the patient develops hypovolaemic shock.

**Question 9 of 206**

A 68-year-old woman was admitted to hospital with severe acute dyspnoea. She denied having any chest pain but said that she had become progressively breathless over the past three months.

On examination, her pulse was 120 beats per minute and regular. Her blood pressure was 95/55 mmHg and her jugular venous pressure was elevated to the angle of the jaw. Her heart sounds were normal. Auscultation of her chest revealed bilateral fine inspiratory crackles to the mid zones. She had haemorrhages in both fundi.

Investigations revealed:

<b>Haemoglobin</b>	56 g/L	(115-165)
<b>Haematocrit</b>	0.19	(0.36-0.47)
<b>MCV</b>	118 fL	(80-96)
<b>MCH</b>	33.0 pg	(28-32)
<b>White cell count</b>	$3.4 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$95 \times 10^9/\text{L}$	(150-400)
<b>Serum vitamin B12</b>	Result pending	
<b>Serum folate</b>	Result pending	

The ECG showed left bundle branch block, which had been documented previously.

She is given 80 mg of intravenous furosemide which results in an excellent diuresis.

Which of the following is the next most appropriate immediate step in her management?

(Please select 1 option)

<input type="radio"/>	Blood transfusion
<input type="radio"/>	Bone marrow aspiration
<input type="radio"/>	Start intramuscular vitamin B12 and oral folic acid
<input type="radio"/>	Start oral ferrous sulphate
<input type="radio"/>	Thrombolyse with t-PA

<input checked="" type="radio"/>	Blood transfusion <b>This is the correct answer</b>
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The clinical picture represents severe megaloblastic anaemia with cardiac failure.

The question asks about immediate management. Although the anaemia has been developing slowly, she has become acutely haemodynamically compromised. In such circumstances, it would be most appropriate to transfuse the patient. This would need to be done very cautiously with diuretic cover.

She will clearly need to start an intensive course of intramuscular vitamin B12 and oral folic acid as well, but this is less important in the hyperacute situation where there is a risk of the patient dying from anaemia.

Giving oral folic acid without vitamin B12 would be hazardous and could precipitate subacute combined degeneration of the spinal cord.

Transfusion may also be hazardous in a patient with severe congestive cardiac failure (CCF).

### Question 10 of 206

Which of the following is most commonly associated with prolonged QT interval?

(Please select 1 option)

<input type="radio"/>	Hypercalcaemia
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<input type="radio"/>	Hyperthyroidism
<input type="radio"/>	Hypocalcaemia
<input type="radio"/>	Hypermagnesaemia
<input type="radio"/>	Hyponatraemia

<input checked="" type="radio"/>	Hypocalcaemia <b>Correct</b>
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Hypocalcaemia causes prolonged QT interval due to an increase in ST segment duration.

Other causes of prolonged QT interval are:

- Hypothermia
- Hypothyroidism
- Drugs (amiodarone)
- Acute myocarditis
- Cerebral injury
- Mitral valve prolapse
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Hypokalemia, and
- Hypomagnesaemia.

### Question 11 of 206

A 45-year-old Chinese man is found incidentally to have a severely hypochromic and microcytic blood picture, with Hb 112 g/L. He is asymptomatic.

Which of the following is the most discriminatory investigation?

(Please select 1 option)

<input type="radio"/>	Barium enema
<input type="radio"/>	Bone marrow biopsy

<input type="radio"/>	Gastroscopy
<input type="radio"/>	Haemoglobin electrophoresis
<input type="radio"/>	Ham test

<input checked="" type="radio"/>	Haemoglobin electrophoresis <b>This is the correct answer</b>
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This patient is most likely to have thalassaemia trait. He has severely microcytic, hypochromic cells but is asymptomatic with a relatively normal haemoglobin. If this were iron deficiency we would expect a much lower haemoglobin, with at least some symptoms.

Beta-thalassaemia trait is associated with minor suppression of beta-chain manufacture and a microcytic hypochromic anaemia, where the MCV is surprisingly low for the level of haemoglobin (which is usually over 90 g/L). An elevated HbA2 (+/- HbF) is a useful marker of this trait.

Alpha-thalassaemia trait results in a more complex clinical picture, as four chains control alpha-chains. The milder cases manifest with microcytosis without anaemia, whereas the more severe case have a microcytic anaemia with splenomegaly and HbH in red cells.

The Ham test is used to diagnose paroxysmal nocturnal haemoglobinuria, which this presentation is not consistent with.

### Question 12 of 206

In sickle cell disease, which of the following is correct?

(Please select 1 option)

<input type="radio"/>	Exchange transfusions prior to major surgery on HbSS patients aims to lower the HbS concentration to 60%
<input type="radio"/>	It is caused by the substitution of glutamic acid by valine at position 4 on the beta chain of haemoglobin

<input type="radio"/>	The erythrocytes of haemoglobin AS patients can sickle at a pO <sub>2</sub> of 5-6 kPa (40-50 mmHg)
<input type="radio"/>	The erythrocytes of haemoglobin SC patients may sickle at a pO <sub>2</sub> of 4 kPa (30 mmHg)
<input type="radio"/>	The Sickledex test involves adding a reagent to blood which allows the nature of the haemoglobinopathy to be determined

<input checked="" type="radio"/>	The erythrocytes of haemoglobin SC patients may sickle at a pO <sub>2</sub> of 4 kPa (30 mmHg) <b>This is the correct answer</b>
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Sickle cell disease in a haemoglobinopathy is caused by the substitution of glutamic acid by valine at position 6 (from the N-terminal) of the beta chain.

It is inherited as an autosomal gene, heterozygous (HbAS) and homozygous (HbSS) forms exist.

A low partial pressure of oxygen (PO<sub>2</sub>) causes HbS to polymerise and precipitate resulting in sickling of the erythrocyte. HbSS patients sickle at PO<sub>2</sub> of 5-6 kPa and HbAS patients sickle at PO<sub>2</sub> of 2.5-4 kPa.

A mild disease is produced when heterozygotes for HbS combine with other haemoglobins, for example, haemoglobin C, thus creating HbSC. Sickling occurs at around 4 kPa.

Diagnosis of sickle cell disease requires the detection of HbS.

The Sickledex test involves the addition of reagent to blood; turbidity confirming the presence of HbS, but it gives no information on other haemoglobins.

Haemoglobin electrophoresis is the only investigation that determines the nature of the haemoglobinopathy.

### Question 13 of 206

In porphyria, which of the following is least likely to precipitate an acute attack?

(Please select 1 option)

<input type="radio"/>	Aspirin
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<input type="radio"/>	Menstruation
<input type="radio"/>	Phenytoin
<input type="radio"/>	Starvation
<input type="radio"/>	Thiopentone
<input checked="" type="radio"/>	Aspirin This is the correct answer

Porphyria is a group of diseases characterised by excess production and excretion of porphyrins and their precursors.

They are caused by enzyme defects within the haem metabolic pathway.

Stress, infection, pregnancy, menstruation, starvation, and certain drugs may precipitate acute attacks.

Definite precipitants include sulphonamides, barbiturates, and phenytoin.

#### Question 14 of 206

Exam Themes May 2002

A 75-year-old man has a history of chronic lymphocytic leukaemia. He has had treatment with several courses of chemotherapy and has now been admitted to hospital with pneumonia.

His medical history revealed that he had suffered several previous upper respiratory tract infections over the previous six months.

Which of the following components of his immune system is likely to be deficient?

(Please select 1 option)

<input type="radio"/>	Complement
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<input type="radio"/>	Immunoglobulin G
<input type="radio"/>	Macrophages
<input type="radio"/>	Mast cells
<input type="radio"/>	T lymphocytes
<input checked="" type="radio"/>	Immunoglobulin G <b>This is the correct answer</b>

Chronic lymphocytic leukaemia (CLL) is commonly complicated by panhypogammaglobulinaemia.

Although intravenous immunoglobulin prevents recurrent infections it does not prolong survival.

### Question 15 of 206

A 35-year-old woman with a history of recurrent anaemia was noted to have target cells and Howell-Jolly bodies on a blood film examination.

Investigations revealed:

<b>Haemoglobin</b>	70 g/L	(115-165)
<b>MCV</b>	77 fL	(80-96)
<b>MCH</b>	26.2 pg	(28-32)
<b>Serum B12</b>	140 µg/L	(160-760)

<b>Red cell folate</b>	95 µg/L	(160-640)
<b>Serum ferritin</b>	10 µg/L	(15-300)

Which disease-specific antibody is most likely to be present?

(Please select 1 option)

<input type="radio"/>	Anti-gastric parietal cell
<input type="radio"/>	Anti-glutamic acid decarboxylase
<input type="radio"/>	Anti-intrinsic factor
<input type="radio"/>	Anti-mitochondrial
<input type="radio"/>	Anti-tissue transglutaminase

<input checked="" type="radio"/>	Anti-tissue transglutaminase <b>This is the correct answer</b>
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The patient has hyposplenism as suggested by the blood film and a mixed anaemia.

Coeliac disease could, therefore, fit the above picture with anti-TTG antibodies being the most appropriate selection from the above list.

- Anti-mitochondrial antibodies are seen in PBC.
- Anti-gastric and anti-intrinsic Abs are seen in pernicious anaemia.
- Anti-GAD abs are found in auto-immune DM.

Screening for coeliac disease should include high-risk groups such as anaemia (iron or folate deficiency), hyposplenism, reduced bone density, and infertility.

**Question 16 of 206**

A 24-year-old male presents after developing a bluish discolouration of the body, lips and nails. He denies any relevant past medical history.

Examination reveals a central cyanosis and a grey complexion.

Investigation revealed:

<b>Haemoglobin</b>	170 g/L	(130-180)
<b>PaO<sub>2</sub></b>	13.0 kPa	(11.3-12.6)
<b>SaO<sub>2</sub> (using an oximeter)</b>	85%	(>95)

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Argyria
<input type="radio"/>	Cyanotic congenital heart disease
<input type="radio"/>	Haemochromatosis
<input type="radio"/>	Methaemoglobinaemia
<input type="radio"/>	Methylene blue poisoning
<input checked="" type="radio"/>	Methaemoglobinaemia <b>This is the correct answer</b>

This patient is otherwise well and has no specific features of congenital heart disease (clubbing, etc).

He appears desaturated with saturations of 85%, yet good pO<sub>2</sub>. This is a typical description of [methaemoglobinaemia](#), which is the accumulation of reversibly oxidised methaemoglobin causing reduced oxygen affinity of the Hb molecule with consequent cyanosis. It can occur due to an inherited condition or as a consequence of drugs such as nitrates.

[Argyria](#) is colloidal silver toxicity.

### Question 17 of 206

A 30-year-old woman presents with a deep vein thrombosis.

Of note in her past medical history is three early miscarriages.

Investigations revealed:

<b>Haemoglobin</b>	128 g/L	(115-165)
<b>White cell count</b>	$3.6 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$35 \times 10^9/\text{L}$	(150-400)

What investigation is most likely to be abnormal?

(Please select 1 option)

<input type="radio"/>	Antiphospholipid antibodies
<input type="radio"/>	Homocystine concentration
<input type="radio"/>	Indium-labelled white cell scan
<input type="radio"/>	Platelet function test
<input type="radio"/>	Protein C concentration



Antiphospholipid antibodies **This is the correct answer**

The combination of thrombophilia, recurrent miscarriage, thrombocytopenia and leucopenia in this patient indicates a diagnosis of antiphospholipid syndrome, probably in association with systemic lupus erythematosus.

Antiphospholipid syndrome is a common cause of acquired thrombophilia and characterised by arterial and/or venous thrombosis and pregnancy mortality in association with circulating antiphospholipid antibodies. These are a heterogeneous group of approximately twenty autoantibodies directed against phospholipid binding plasma proteins. Three of the most clinically important are the lupus anticoagulant, anti-beta-2 glycoprotein I antibodies and the anticardiolipin antibodies. They can be detected either by phospholipid-dependent coagulation test for lupus anticoagulant or ELISA test for anticoagulation and anti-β2GPI antibodies. Antibodies should be demonstrated on at least two occasions separated by 12 weeks. Antiphospholipid syndrome may be primary, or associated with other conditions (such as systemic lupus erythematosus).

Antiphospholipid syndrome is the most important treatable cause of recurrent miscarriage, defined as the loss of three or more consecutive pregnancies. 15% of women with recurrent miscarriage have persistently positive tests for either lupus anticoagulant or anticardiolipin antibodies, compared to 2% with an uncomplicated obstetric history. In future untreated pregnancies, women with recurrent miscarriage and persistently positive anticardiolipin antibodies have a miscarriage rate of 90%. The majority of miscarriages occur between 7 and 12 weeks gestation, and fetuses are typically chromosomally normal. It is thought the antibodies affect trophoblast invasion and placentation.

Antiphospholipid syndrome is also an important cause of early onset pre-eclampsia and intra-uterine growth restriction.

Aspirin and low-dose heparin is the treatment of choice to reduce the risk of miscarriage in confirmed antiphospholipid syndrome. This combination has been shown to lead to a 70% live birth rate in future pregnancies. Intravenous immunoglobulin can also be used.

Elevated levels of circulating homocysteine increase the risk of developing coronary artery disease, peripheral vascular disease and cerebrovascular disease but they are not commonly associated with pregnancy loss.

An indium white blood cell scan is a nuclear medicine study in which leucocytes are removed from the patient, tagged with Indium-111 and reinjected into the patient. They can then be

used to localise areas of infection and inflammation, such as thrombophlebitis and osteomyelitis.

Platelet function studies measure the platelet's ability to adhere and aggregate. They are not particularly reliable or accurate, and therefore do not have a central role in clinical practice.

Protein C is one of the major inhibitors of the coagulation system. Deficiency is associated with an increased risk of venous thrombosis, but not classically an increase rate of miscarriage.

### Question 18 of 206

A 68-year-old man complained of tiredness and lethargy.

On examination there was 2 cm hepatomegaly and 7 cm splenomegaly.

Investigations show:

<b>Haemoglobin</b>	174 g/L	(130-180)
<b>White cell count</b>	$39.4 \times 10^9/\text{L}$	(4-11)

White cell differential:

<b>Neutrophils</b>	$22.2 \times 10^9/\text{L}$	(1.5-7)
<b>Lymphocytes</b>	$1.1 \times 10^9/\text{L}$	(1.5-4)
<b>Monocytes</b>	$1.0 \times 10^9/\text{L}$	(0-0.8)
<b>Eosinophils</b>	$0.4 \times 10^9/\text{L}$	(0.04-0.4)
<b>Basophils</b>	$2.1 \times 10^9/\text{L}$	(0-0.1)
<b>Metamyelocytes</b>	$1.2 \times 10^9/\text{L}$	-

<b>Myelocytes</b>	$10.9 \times 10^9/L$	-
<b>Myeloblasts</b>	$1.3 \times 10^9/L$	-
<b>Nucleated RBC</b>	3 per 100 rbc	-
<b>Platelet count</b>	$585 \times 10^9/L$	(150-400)

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Chronic myeloid leukaemia (CML)
<input type="radio"/>	Essential thrombocythaemia
<input type="radio"/>	Myelofibrosis
<input type="radio"/>	Primary proliferative polycythaemia (rubra vera)
<input checked="" type="radio"/>	Chronic myeloid leukaemia (CML) <b>This is the correct answer</b>

The presentation is typical with vague symptoms of malaise and splenomegaly.

The blood film also shows the typical high white cell count and there are all stages of myeloid cell maturation present in the peripheral blood with the metamyelocytes suggesting CML.

Thrombocythaemia is also seen in CML.

### Question 19 of 206

An 18-year-old Asian female is noted by her dentist to have gingival hypertrophy.

Which of the following is most likely to be responsible for her presentation?

(Please select 1 option)

<input type="radio"/>	Carbamazepine
<input type="radio"/>	Lead poisoning
<input type="radio"/>	Phenytoin
<input type="radio"/>	Scurvy
<input type="radio"/>	Sodium valproate

<input checked="" type="radio"/>	Phenytoin This is the correct answer
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The inclusion of 'Asian' descent in this question is intended as a distractor.

Gum hypertrophy may be seen in conditions such as acute myeloid leukaemias and with drugs such as phenytoin. Of the options here, phenytoin is the most likely.

Scurvy (vitamin C deficiency) can be associated with swollen, bleeding gums which can become friable and infected, but true gingival hypertrophy is not classic. Petechiae can occur on the mucosae.

Lead toxicity is associated with pigmentation of the gingiva.

Carbamazepine is not associated with gingival hyperplasia but recognised side effects include ataxia, drowsiness and blood dyscrasias.

### Question 20 of 206

Which of the following is a proto-oncogene?

(Please select 1 option)

<input type="radio"/>	The BCRabI translocation (Philadelphia chromosome)
<input type="radio"/>	The N-Myc gene
<input type="radio"/>	The retinoblastoma gene
<input type="radio"/>	The WT1 (first Wilm's tumour) gene
<input type="radio"/>	The WT2 (second Wilm's tumour) gene
<input checked="" type="radio"/>	The N-Myc gene <b>This is the correct answer</b>

Oncogenes are endogenous human deoxyribonucleic acid (DNA) sequences that arise from normal genes called proto-oncogenes.

Proto-oncogenes are normally expressed in many cells, particularly during fetal development, and are thought to play an important regulatory role in cell growth and development.

Alterations in the proto-oncogene can activate an oncogene, which produces unregulated gene activity, contributing directly to tumourogenesis.

Oncogene alterations are important causes of:

- Rhabdomyosarcomas (ras oncogene)
- Burkitt's lymphoma (C-myc is translocated intact from its normal position on chromosome 8 to chromosome 14)
- Neuroblastoma (N-myc proto-oncogene is seen in a proportion of patients with poor prognosis).

They should be contrasted with tumour suppressor genes. In this situation, the genes normally down-regulate cell growth, and require inactivation to allow malignant growth. Examples include retinoblastoma.

### Question 21 of 206

Which of the following conditions is most likely to be associated with thrombocytopenia?

(Please select 1 option)

<input type="radio"/>	Haemophilia A
<input type="radio"/>	Hereditary haemorrhagic telangiectasia
<input type="radio"/>	Pernicious anaemia
<input type="radio"/>	Porphyria
<input type="radio"/>	Uraemia

<input checked="" type="radio"/>	Pernicious anaemia <b>This is the correct answer</b>
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Pernicious anaemia is usually a megaloblastic anaemia but may also be associated with a pancytopenia.

The platelet count is usually normal in chronic renal failure but there is a platelet function abnormality.

### Question 22 of 206

Which of the following is a feature of hereditary haemorrhagic telangiectasia?

(Please select 1 option)

<input type="radio"/>	A good response to oestrogen therapy
<input type="radio"/>	Cerebral arteriovenous malformations
<input type="radio"/>	GI haemorrhage is the usual presenting feature
<input type="radio"/>	Telangiectasia of the mucous membranes, but not the skin

<input type="radio"/>	Tendency of lesions to become less obvious with age
<input checked="" type="radio"/>	Cerebral arteriovenous malformations <b>This is the correct answer</b>

Hereditary haemorrhagic telangiectasia (HHT) is a multisystem vascular dysplasia characterised by the presence of multiple arteriovenous malformations (AVMs) that lack intervening capillaries and result in direct connections between arteries and veins. Small AVMs, called telangiectases, close to the surface of skin and mucous membranes often rupture and bleed. It is inherited as an autosomal dominant trait.

The most common clinical manifestations of HHT are spontaneous and recurrent epistaxis and multiple telangiectases which commonly appear on the lips, face, tongue, or hands in adulthood. A minority of individuals with HHT have symptomatic gastrointestinal bleeding, which most commonly begins after age 50 years.

Large AVMs often cause symptoms when they occur in the brain or lung; complications from bleeding or shunting may be sudden and catastrophic. It is estimated at least 30% of HHT patients have pulmonary involvement, 30% hepatic involvement, and 10-20% cerebral involvement.

The manifestations of HHT generally develop with age and are usually not present at birth. Epistaxis is usually the earliest sign of disease, often occurring in childhood. Pulmonary AVMs can become apparent from puberty. By the age of 16 years, 71% of patients will have developed signs of HHT, rising to over 90% by 40 years.

The Curacao criteria can be used to aid diagnosis:

The diagnosis is:

- 'definite' if three criteria are present
- 'possible' or 'suspected' if two criteria are present, or
- 'unlikely' if fewer than two criteria are present.

Criteria are:

- epistaxis: spontaneous, recurrent nose bleeds
- telangiectases: multiple, characteristic sites (lips, oral cavity, fingers, nose)
- visceral lesions, such as gastrointestinal telangiectasia, pulmonary AVM, hepatic AVM, cerebral AVM, spinal AVM, and

- family history of a first-degree relative with HHT.

Cerebral involvement can be in the form of telangiectasias, cerebral AVMs, aneurysms, or cavernous angiomas. Cerebral AVMs are thought to affect 10% of patients and can result in headaches, seizures, surrounding ischaemia (steal), or haemorrhage. These lead to significant mortality and morbidity.

Management of epistaxis and gastrointestinal haemorrhage should be symptomatic initially. Whilst it is generally regarded that pulmonary AVMs should be screened for (and treated with prophylactic antibiotics and embolisation), screening for cerebral and hepatic AVMs remains controversial and is not currently offered in the UK. Oestrogen therapy is sometimes advocated but its efficacy is unclear. It may be beneficial in heavily transfusion dependent patients

### Question 23 of 206

Which of the following statements is true of sickle cell disease?

(Please select 1 option)

<input type="radio"/>	A painful shoulder joint will respond to intra-articular corticosteroid injection
<input type="radio"/>	Oral iron supplements are required
<input type="radio"/>	Symptoms of anaemia are usually limiting when haemoglobin equals 80 g/L
<input type="radio"/>	There is often an inability to concentrate urine
<input type="radio"/>	The spleen is frequently enlarged
<input checked="" type="radio"/>	There is often an inability to concentrate urine <b>This is the correct answer</b>

A urine concentrating defect is quite common in sickle cell anaemia, has its onset in early childhood, and may be reversible with prevention of sickle crises. The inner medulla is hypoxic, hypertonic and acidotic and therefore predisposes to sickling of red blood cells, which results in vasoocclusion and reduction in renal medullary blood flow. Associated haematuria increases venous pressure, which can worsen renal medulla ischaemia. Clinical manifestations depend on the predominant site of tubule involvement: proximal tubule dysfunction impairs urinary concentration, whilst more distal dysfunction impairs potassium excretion.

There is a tendency to iron overload in sickle cell disease and therefore iron therapy is not usually indicated. The spleen is decreased in size after six months of age, due to repeated episodes of venoocclusion and infarction, and patients often have functional hyposplenism and are recommended to take daily penicillin. The anaemia associated with sickle cell disease is usually only symptomatic below 70 g/L, as oxygen is released more readily from erythrocytes. Intra-articular steroids have been associated with a sickle cell crisis, the mechanism of which is not fully understood, but they should be avoided.

#### Question 24 of 206

A 41-year-old African man has a history of multiple episodes of sudden onset of severe abdominal pain and back pain lasting for hours. Each time this happens, his peripheral blood smear demonstrates numerous sickled erythrocytes.

A haemoglobin electrophoresis shows:

<b>Hgb S</b>	94%
<b>Hgb F</b>	5%
<b>Hgb A2</b>	1%

He now has increasing pain in his right groin radiating to the anterior aspect of the thigh and to the knee. His temperature was 38°C and examination of his hip revealed pain on internal rotation. A radiograph reveals irregular bony destruction of the femoral head.

What is the organism most likely to be responsible for these findings?

(Please select 1 option)

<input type="radio"/>	<i>Candida albicans</i>
<input type="radio"/>	<i>Clostridium perfringens</i>
<input type="radio"/>	Group B <i>Streptococcus</i>
<input type="radio"/>	<i>Salmonella</i> species
<input type="radio"/>	<i>Yersinia pestis</i>
<input checked="" type="radio"/>	<i>Salmonella</i> species This is the correct answer

*Salmonella* osteomyelitis is seen in patients with sickle cell anaemia.

Other organisms that are frequent causes for osteomyelitis with sickle cell anaemia include *Staphylococcus aureus* and Gram negatives such as *Klebsiella*.

Why *Salmonella* species predominate in patients with sickle cell disease instead of *Staphylococcus aureus* is a matter of debate.

### Question 25 of 206

Which of the following statements relates to acquired sideroblastic anaemia?

(Please select 1 option)

<input type="radio"/>	Haemosiderinuria is a feature
<input type="radio"/>	Has increased methaemoglobinaemia
<input type="radio"/>	It is characterised by the presence of ringed sideroblasts in the peripheral blood

<input type="radio"/>	It shows increased haptoglobin
<input type="radio"/>	There may be some response to pyridoxine therapy

<input checked="" type="radio"/>	There may be some response to pyridoxine therapy <b>This is the correct answer</b>
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Sideroblasts are found in marrow.

Haptoglobin falls during haemolysis and may climb with 'acute phase' response.

There is an occasional response to pyridoxine.

Methaemoglobinaemia and haemosiderinuria are features of intravascular haemolysis.

### Question 26 of 206

Which single statement is true regarding the treatment of iron deficiency anaemia?

(Please select 1 option)

<input type="radio"/>	Absorption of iron is increased by ascorbic acid
<input type="radio"/>	Ferrous sulphate 200 mg has less elemental iron than the same dose of ferrous gluconate
<input type="radio"/>	Iron is absorbed in the distal jejunum
<input type="radio"/>	Parenteral iron is indicated when the anaemia responds slowly to oral iron
<input type="radio"/>	Sustained release iron is a useful way of giving larger doses



Absorption of iron is increased by ascorbic acid **This is the correct answer**

Absorption of oral iron is improved by ascorbic acid.

Ferrous sulphate has more elemental iron by mass.

Iron is absorbed in the upper small intestine.

Parenteral iron acts no faster than oral iron. It is indicated when oral iron cannot be tolerated or is not absorbed.

Sustained-release preparations may improve tolerance of oral iron but do not aid absorption.

### Question 27 of 206

A 55-year-old male presents with anorexia and weight loss of 12 months duration. Over this year he has had two deep vein thromboses (DVTs) and had the last whilst his INR was 2 (less than 1.4).

He remains on long-term warfarin therapy with an INR above 2.6. Examination reveals a postural drop in his blood pressure of 15 mmHg and discolouration of his palmar creases and around his lips.

Investigations are as follows:

<b>Sodium</b>	131 mmol/L	(137-144)
<b>Potassium</b>	5.0 mmol/L	(3.5-4.9)
<b>INR</b>	3.0	(<1.4)

A short Synacthen test reveals a baseline cortisol concentration at time 0 of 120 nmol/L which rises to 155 nmol/L after 30 minutes (normal response greater than 550 nmol/L).

Which single diagnosis would explain this patient's illness?

(Please select 1 option)



Addison's disease

<input type="radio"/>	Antiphospholipid syndrome
<input type="radio"/>	Autoimmune polyendocrine syndrome (Schmidt's disease)
<input type="radio"/>	Pituitary infarction
<input type="radio"/>	Protein S deficiency
<input checked="" type="radio"/>	Antiphospholipid syndrome <b>This is the correct answer</b>

With a history of recurrent DVT and confirmed hypoadrenalism, this patient is likely to have antiphospholipid syndrome. Antiphospholipid syndrome is a primary diagnosis or may co-exist with systemic lupus erythematosus. In this case, it is likely to have caused adrenal infarcts which have resulted in hypoadrenalism.

Anticardiolipin antibodies or lupus anticoagulant may be present.

It is associated with arterial and venous thrombosis and has a predilection for the adrenal veins causing adrenal infarction with consequent hypoadrenalism.

Addison's disease is an autoimmune phenomenon and is not associated with DVT.

The pigmentation, which is due to increased adrenocorticotrophic hormone (ACTH) in hypoadrenalism, would exclude pituitary infarction as the cause of the hypoadrenalism.

Hypoadrenalism is not associated with protein S deficiency.

Autoimmune polyendocrine syndrome is associated with:

- hypothyroidism
- type 1 diabetes, and
- Addison's disease.

### Question 28 of 206

An 80-year-old woman has a three-month history of progressive numbness and unsteadiness of her gait. She has a history of hypertension which is controlled with indapamide and lisinopril and diet controlled diabetes but is otherwise well.

On examination her BP is 132/82, pulse is 75 and regular, heart sounds are normal, abdomen is soft and non-tender, and her BMI is 23. There is a mild spastic paraparesis, with brisk knee reflexes, ankle reflexes are present with reinforcement, extensor plantars, sensory loss in the legs with a sensory level at T10, impaired joint position sense in the toes, and loss of vibration sense below the iliac crests.

Investigations were as follows:

<b>Haemoglobin</b>	122 g/L	(120-160)
<b>MCV</b>	95 fL	(80-96)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Anterior spinal artery occlusion
<input type="radio"/>	Dorsal meningioma
<input type="radio"/>	Multiple sclerosis
<input type="radio"/>	Subacute combined degeneration of the cord
<input type="radio"/>	Tabes dorsalis
<input checked="" type="radio"/>	Dorsal meningioma <b>This is the correct answer</b>

The presence of a sensory loss at T10 indicates a thoracic myelopathy.

Sub-acute combined degeneration of the cord is unlikely as the haemoglobin concentration and mean corpuscular volume (MCV) are normal, there is also no history suggestive of autoimmune disease to raise the possibility of pernicious anaemia.

Anterior spinal artery occlusion is unlikely as the history is progressive and chronic, whereas weakness related to anterior spinal artery occlusion occurs over a period of approximately 6-12 hours.

Tabes dorsalis is also associated with cognitive impairment and global degeneration, rather than the sensory level seen here.

Multiple sclerosis typically presents before the age of 60. Whilst there is a primary progressive form, most commonly it presents with acute neurological deficits which then resolve (fully or partially) to be followed by subsequent events months or years later. The pattern of disease and the age of the patient is therefore not consistent with a diagnosis of MS here.

### Question 29 of 206

A 67-year-old woman presents with acute severe back pain. She is normally fit and well, but there is a strong family history of osteoporosis.

<b>Hb</b>	106 g/L	(120-160)
<b>MCV</b>	85 fL	(80-90)
<b>Calcium</b>	2.9 mmol/L	(2.2-2.6)
<b>Phosphate</b>	2.2 mmol/L	(0.8-1.2)
<b>Alkaline phosphatase</b>	126 IU/L	(50-150)
<b>Total protein</b>	76 g/L	(60-83)
<b>Albumin</b>	30 g/L	(35-45)

What is the most likely underlying diagnosis?

(Please select 1 option)

<input type="radio"/>	Metastatic disease
<input type="radio"/>	Multiple myeloma
<input type="radio"/>	Osteoporosis
<input type="radio"/>	Paget's disease
<input type="radio"/>	Sarcoidosis

<input checked="" type="radio"/>	Multiple myeloma This is the correct answer
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This patient has hypercalcaemia/hyperphosphataemia and hyperglobulinaemia. The globulin level is raised at 46 g/L (globulin level = total protein – albumin. In this case, 76 – 30 = 46). A normal level should be below 36 g/L.

This together with normocytic anaemia and probable vertebral collapse would be highly suggestive of multiple myeloma.

She needs serum immunoelectrophoresis, urinary Bence-Jones protein and bone marrow biopsy.

The hyperphosphataemia in multiple myeloma is due to reduced renal excretion which may be directly due to renal impairment or interference with excessive protein load.

### Question 30 of 206

Which of the following patients with Hodgkin's disease has the worst prognosis?

(Please select 1 option)

<input type="radio"/>	25-year-old man with cervical and mediastinal lymphadenopathy
<input type="radio"/>	25-year-old man with inguinal lymphadenopathy

<input type="radio"/>	25-year-old man with mediastinal and inguinal lymphadenopathy and pruritus
<input type="radio"/>	25-year-old woman with mediastinal and inguinal lymphadenopathy
<input type="radio"/>	25-year-old woman with mediastinal and inguinal lymphadenopathy and night sweats
<input checked="" type="radio"/>	25-year-old woman with mediastinal and inguinal lymphadenopathy and night sweats <b>This is the correct answer</b>

Prognosis in Hodgkin's disease depends on staging and presence of B symptoms.

The first patient has stage IIA disease (two lymph node areas on same side of diaphragm).

The second patient has Stage IA disease (one lymph node area).

The third and fourth patients have stage IIIA disease (disease in lymph nodes on both sides of diaphragm). Pruritus is not a B symptom and is not of prognostic significance.

The fifth patient has stage IIIB disease (as night sweats are a B symptom).

### Question 31 of 206

Whilst being investigated for infertility, a 30-year-old woman is noted to have some bruising on her limbs with a palpable spleen on abdominal examination.

Investigations reveal:

<b>Haemoglobin</b>	100 g/L	(115-165)
<b>White cell count</b>	$110 \times 10^9/\text{L}$	(4-11)
<b>Neutrophils</b>	$60 \times 10^9/\text{L}$	(1.5-7)

<b>Lymphocytes</b>	$2 \times 10^9/\text{L}$	(1.5-4)
<b>Monocytes</b>	$0.8 \times 10^9/\text{L}$	(0-0.8)
<b>Eosinophils</b>	$0.3 \times 10^9/\text{L}$	(0.04-0.4)
<b>Basophils</b>	$0.7 \times 10^9/\text{L}$	(0-0.1)
<b>Myelocytes</b>	$40 \times 10^9/\text{L}$	-
<b>Myeloblasts</b>	$4 \times 10^9/\text{L}$	-
<b>Platelet count</b>	$900 \times 10^9/\text{L}$	(150-400)

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Acute promyelocytic leukaemia
<input type="radio"/>	Chronic myeloid leukaemia
<input type="radio"/>	Essential thrombocythaemia
<input type="radio"/>	Myelofibrosis



Chronic myeloid leukaemia **This is the correct answer**

The features of this blood film are anaemia, thrombocytosis, neutrophilia with roughly 55% neutrophils, 40% myelocytes with less than 5% blast cells.

This is typical of chronic myeloid leukaemia which usually has associated tender splenomegaly. Usually, the Philadelphia chromosome is present in 95% of cases.

Acute leukaemia is defined as blast cells constituting over 30% of cell type present.

Chronic myeloid leukaemia often ends in acute blastic transformation after a mean duration of approximately four years.

### Question 32 of 206

A 60-year-old male presents with bruising and tiredness.

Examination reveals four finger breadth splenomegaly and his results reveal:

<b>Haemoglobin</b>	110 g/L	(130-180)
<b>White cell count</b>	$100 \times 10^9/L$	(4-11)
<b>Platelets</b>	$900 \times 10^9/L$	(150-400)

Blood film reveals a neutrophilia, basophilia, numerous myelocytes and 4% myeloblasts.

Which of the following is likely to be present in this patient?

(Please select 1 option)



BCR-ABL gene fusion only



Deletion 11q13



Deletion chromosome 13

<input type="radio"/>	Normal chromosomal analysis
<input type="radio"/>	Translocation 9;22
<input checked="" type="radio"/>	Translocation 9;22 <b>This is the correct answer</b>

The Philadelphia chromosome (translocation 9;22) is present in approximately 90% of subjects with chronic myelocytic leukaemia (CML).

The molecular consequences of this translocation is the generation of the fusion bcr-abl gene which creates an abnormal protein stimulating white cell growth. Only 5% of cases have the bcr-abl fusion gene only without the typical Philadelphia chromosome.

Deletion of Ch13 is associated with a poorer prognosis in multiple myeloma.

### Question 33 of 206

Which of the following statements concerning iron metabolism is correct?

(Please select 1 option)

<input type="radio"/>	Approximately 0.1% of body iron circulates in the plasma
<input type="radio"/>	Approximately 90% of dietary iron is absorbed in the intestine
<input type="radio"/>	The main route of excretion is the liver
<input type="radio"/>	The serum ferritin concentration is reduced characteristically following surgery
<input type="radio"/>	The transferrin content of intestinal mucosal cells is high when body iron stores are high



Approximately 0.1% of body iron circulates in the plasma **Correct**

Approximately 4 mg of iron circulate within the plasma with a total body iron store of 3-4 g (2500 mg in the RBCs, 500 mg in liver, 500 mg in macrophages, and about 500 mg in muscle).

From an intake of approximately 6 mg/1000 kcal of dietary iron, only 15% is bioavailable.

The majority of iron contained within the RBCs is metabolised and re-utilised but 1 mg per day is lost through the gut.

Ferritin, the plasma protein responsible for binding iron, is an acute phase reactant protein and increases in inflammatory conditions following surgery.

Transferrin is a glycoprotein responsible for internal iron exchange and the content within mucosal cells is naturally low in haemochromatosis with high saturation.

### Question 34 of 206

A 42-year-old female presents with tiredness. She does not take any regular medications, smoke or drink alcohol. Her investigations reveal:

<b>Haemoglobin</b>	78 g/L	(115-165)
<b>MCV</b>	72 fL	(80-96)
<b>White cell count</b>	$7.6 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$350 \times 10^9/\text{L}$	(150-400)
<b>Serum ferritin</b>	8 $\mu\text{g/L}$	(15-300)

She was commenced on oral iron therapy and one month later her haemoglobin concentration was 80 g/L (115-165).

What is the most likely cause of the failure of her haemoglobin to respond to this treatment?

(Please select 1 option)

<input type="radio"/>	Acquired sideroblastic anaemia
<input type="radio"/>	Coeliac disease
<input type="radio"/>	Folate deficiency
<input type="radio"/>	Inadequate dosage of iron
<input type="radio"/>	Poor compliance with therapy

<input checked="" type="radio"/>	Poor compliance with therapy <b>This is the correct answer</b>
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The most likely explanation for the failure of an iron deficiency anaemia to respond to iron therapy in a menstruant female is poor compliance. It is likely that the dose that this patient is prescribed would be adequate and if not some response would still be expected.

There is no evidence of a concomitant folate deficiency as suggested by the blood picture, which would also argue against coeliac disease.

Similarly, there is no evidence to suggest an acquired sideroblastic anaemia where a raised MCV and increased ferritin may be expected.

### Question 35 of 206

A 70-year-old female presents for investigation of fatigue and weight loss.

Investigations reveal:

<b>Haemoglobin</b>	90 g/L	(115-165)
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<b>White cell count</b>	2.0 ×10 <sup>9</sup> /L	(4-11)
<b>Platelet count</b>	250 ×10 <sup>9</sup> /L	(150-400)
<b>Total protein</b>	74 g/L	(61-76)
<b>Albumin</b>	28 g/L	(37-49)
<b>Urea</b>	16 mmol/L	(2.5-7.5)
<b>Creatinine</b>	250 µmol/L	(60-110)
<b>Plasma glucose</b>	6.5 mmol/L	(3.0-6.0)
<b>Urine dipstick analysis</b>	Protein+	
	Blood+	
<b>Renal ultrasound</b>	Normal	

Which one of the following investigations would be most appropriate for this patient?

(Please select 1 option)

<input type="radio"/>	24-hour urinary protein estimation
<input type="radio"/>	Measurement of anti-glomerular basement membrane (anti-GBM) antibodies

<input type="radio"/>	Measurement of anti-neutrophil cytoplasmic antibodies (ANCA)
<input type="radio"/>	Plasma protein electrophoresis
<input type="radio"/>	Renal angiography

<input checked="" type="radio"/>	Plasma protein electrophoresis <b>This is the correct answer</b>
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This patient may well have myeloma as reflected by the anaemia, leucopenia, and elevated non-albumin protein concentration.

Thus plasma protein electrophoresis would be the investigation of choice in this patient.

### Question 36 of 206

A 70-year-old male is admitted with haematemesis. He is currently being treated with warfarin for atrial fibrillation and his INR returns as 10.

Which of the following is the most appropriate immediate treatment of his INR?

(Please select 1 option)

<input type="radio"/>	Cryoprecipitate
<input type="radio"/>	Fresh frozen plasma
<input type="radio"/>	Intravenous vitamin K
<input type="radio"/>	Oral vitamin K
<input type="radio"/>	Prothrombin complex concentrate



Prothrombin complex concentrate **This is the correct answer**

This gentleman is having a potentially life-threatening bleed in the setting of a grossly elevated INR.

Due to his warfarin therapy, he will have reduced levels of factors II, VII, IX, and X and requires replacement to correct his INR rapidly. This is most effectively achieved by the administration of prothrombin complex concentrate (Beriplex or Octaplex, 25-50 units/kg IV).

These result in complete reversal of the warfarin-induced anticoagulation within 10 minutes, but the clotting factors have a finite half-life and therefore 5 mg IV vitamin K should be given at the same time.

Fresh frozen plasma (FFP) contains more dilute clotting factors and therefore produces inferior correction and should not be used in the management of life-threatening bleeding (unless prothrombin complex concentrate is not available).

Cryoprecipitate and oral vitamin K are not recommended for the management of life-threatening bleeding.

### Question 37 of 206

Exam Themes January 2006

A 42-year-old man being investigated for diabetes and impotence is noted to have the following results:

<b>Alanine aminotransferase</b>	30 U/L	(5-35)
<b>Aspartate aminotransferase</b>	22 U/L	(1-31)
<b>Fasting plasma glucose</b>	7.4 mmol/L	(3.0-6.0)
<b>Ferritin</b>	500 µg/L	(15-300)

Which one of the following would be the next most appropriate investigation?

(Please select 1 option)

<input type="radio"/>	Bone marrow smear and iron stain
<input type="radio"/>	Liver biopsy
<input type="radio"/>	Red cell protoporphyrins
<input type="radio"/>	Serum transferrin receptors
<input type="radio"/>	Transferrin saturation

<input checked="" type="radio"/>	Transferrin saturation <b>Correct</b>
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This patient has a suspected diagnosis of haemochromatosis as suggested by the presentation and laboratory investigations including elevated ferritin.

The next investigation would be measurement of transferrin saturation, and then, if elevated (above 45%), genotyping (homozygosity for C282y mutations) would next be considered and would be expected to clinch the diagnosis.

In the event of rarer mutations, confirmation with liver biopsy may be required.

### Question 38 of 206

A 42-year-old man presented with tiredness, breathlessness, and nose bleeds for three weeks.

On examination, there were several bruises on his arms and legs, 2 cm splenomegaly and fundal haemorrhages.

Investigations revealed:

<b>Haemoglobin</b>	72 g/L	(130-180)
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<b>White cell count</b>	13.8 ×10 <sup>9</sup> /L	(4-11)
<b>Platelet count</b>	24 ×10 <sup>9</sup> /L	(150-400)
<b>Blood film</b>	White cells predominantly myeloblasts and promyelocytes	

Which one of the following investigations would be of most prognostic value?

(Please select 1 option)

<input type="radio"/>	Bone marrow trephine biopsy
<input type="radio"/>	Cerebrospinal fluid examination
<input type="radio"/>	Cytochemistry
<input type="radio"/>	Cytogenic karyotype
<input type="radio"/>	Immunophenotyping

<input checked="" type="radio"/>	Cytogenic karyotype <b>This is the correct answer</b>
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Cytogenetic evaluation of malignant haematological cells may have important implications for the prognosis and treatment options in acute myelogenous leukaemia (AML).

For example, t(8;21) confers a good prognosis in adult AML, and about 70% of patients in this low-risk group can be cured with intensive chemotherapy alone, radiotherapy being reserved for patients who relapse.

### Question 39 of 206

Exam Themes September 2006

You are called to the Emergency Department to assess a 21-year-old student who has presented with bloody diarrhoea.

The diarrhoea started two weeks previously and was associated with increasing nausea and malaise and mild swelling of the lower limbs. She was having difficulty passing urine. She had eaten steak from the local butcher at a friend's barbeque the day before developing diarrhoea.

On examination, she was pale with evidence of petechiae over her legs. Her face appeared puffy. Blood pressure was 160/95 mmHg. She was afebrile but had a tachycardia and crackles on inspiration at both lung bases. There was an old appendicectomy scar in the right iliac fossa.

Investigations showed:

<b>Haemoglobin</b>	85 g/L	(115-165)
<b>White cell count</b>	$13.2 \times 10^9/\text{L}$	(4-11)
<b>Neutrophils</b>	$9.5 \times 10^9/\text{L}$	(1.5-7)
<b>Platelets</b>	$35 \times 10^9/\text{L}$	(150-400)
<b>PT</b>	12 s	(11.5-15.5)
<b>APTT</b>	34 s	(30-40)
<b>Fibrinogen</b>	4 g/L	(1.8-5.4)
<b>Serum sodium</b>	139 mmol/L	(137-144)
<b>Serum potassium</b>	6.1 mmol/L	(3.5-4.9)

<b>Serum urea</b>	40 mmol/L	(2.5-7.5)
<b>Serum creatinine</b>	411 µmol/L	(60-110)
<b>Serum albumin</b>	27 g/L	(37-49)
<b>Dipstick urine</b>	Blood ++ Protein +	

What is the single most important next investigation to determine the diagnosis?

(Please select 1 option)

<input type="radio"/>	ASO titres
<input type="radio"/>	Blood film analysis
<input type="radio"/>	Renal tract ultrasound
<input type="radio"/>	Transthoracic echocardiogram
<input type="radio"/>	Urine microscopy
<input checked="" type="radio"/>	Blood film analysis <b>Correct</b>

This patient has haemolytic uraemic syndrome (HUS).

It typically presents with a triad of:

- acute renal failure (ARF)
- microangiopathic haemolytic anaemia, and
- thrombocytopenia with normal clotting.

HUS is a complication of infection with verocytotoxin producing *Escherichia coli* usually of the serotype 0157:H7.

Toxins produced in the intestine enter the blood and bind to endothelial cells in target organs. Endothelial cell damage leads to platelet and fibrin deposition with resultant fragmentation of circulating red blood cells and microvascular occlusion.

The syndrome has also been reported after infections with coxsackie, echovirus and *Shigella*.

HUS is characterised by the sudden onset of haemolytic anaemia with fragmentation of red blood cells, thrombocytopenia and acute renal failure after a prodromal illness of acute gastroenteritis often with bloody diarrhoea.

Clinical signs include increasing pallor, haematuria, oliguria and purpura. Jaundice is occasionally seen. Hypertension may be present.

Typical results show an anaemia, thrombocytopenia, and often a neutrophilia. Blood film shows fragmented erythrocytes.

Urea and electrolytes are typical of acute renal failure. There is normal coagulation and fibrinogen.

Neurological complications include:

- stroke, seizure and coma occur in 25% of patients
- rarely pancreatitis, and
- pleural and pericardial effusions.

Approximately 5% of patients will develop end-stage renal failure.

Long-term renal sequelae range from proteinuria to chronic renal failure.

Therapy is supportive with:

- correction of anaemia
- correction of uraemia by early dialysis
- strict fluid balance, and
- treatment of hypertension.

Major differential diagnosis is:

1. Sepsis with DIC - presents with abnormalities of clotting parameters.
2. TTP - thrombotic thrombocytopenic purpura presents with microangiopathic haemolytic anaemia, thrombocytopenic purpura, neurologic abnormalities, fever, and renal disease.

Renal abnormalities tend to be more severe in HUS.

Although once considered variants of a single syndrome, recent evidence suggests that the pathogenesis of TTP and HUS is different. Patients with TTP lack a plasma protease that is responsible for the breakdown of von Willebrand factor (vWF) multimers and these accumulate in the plasma. The activity of this protease is normal in patients with HUS.

Until the test for vWF protease activity becomes available, differentiation between HUS and TTP is based on the presence of central nervous system involvement in TTP and the more severe renal involvement in HUS.

In HUS 90% of patients are children and a history of prodromal diarrhoeal illness is more common.

The therapy of choice for TTP is plasma exchange with fresh frozen plasma.

#### Question 40 of 206

A 32-year-old man was prescribed an oral antibiotic for a urinary tract infection.

Two days later he noticed that his urine was increasingly dark in colour.

Investigations revealed:

<b>Haemoglobin</b>	85 g/L	(130-180)
<b>Reticulocytes</b>	$147 \times 10^9/L$	(25-85)

Blood film: marked anisopoikilocytosis and bite cells.

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Autoimmune haemolytic anaemia
<input type="radio"/>	Haemoglobin H disease
<input type="radio"/>	Hereditary spherocytosis

<input type="radio"/>	Paroxysmal cold haemoglobinuria
<input checked="" type="radio"/>	Autoimmune haemolytic anaemia <span style="color: green;">This is the correct answer</span>

Paroxysmal cold haemoglobinuria (PCH) is a rare type of autoimmune haemolytic anaemia (AIHA) occurring primarily in children.

The classic symptom of PCH is a sudden onset of haemoglobinuria following exposure to cold, even for a few minutes. Symptoms may occur minutes to hours following exposure to cold. Haemoglobinuria is not always present because in some persons with PCH the autoantibody level is not high enough to cause intravascular haemolysis. PCH is usually of abrupt onset in the setting of an infectious disease.

Given the patient's age and the specific history, in this case, the diagnosis is unlikely to be PCH.

If the diagnosis were hereditary spherocytosis then the blood film would show spherocytes.

In haemoglobin H disease the typical inclusions can be demonstrated in erythrocytes stained with brilliant cresyl blue and a chronic microcytic, hypochromic anaemia would be present.

Haemolytic anaemia may be precipitated by sulfonamides and also by penicillins.

This gentleman may have been treated with trimethoprim or a penicillin which then caused AIHA with the typical blood film.

The most appropriate answer to this question is autoimmune haemolytic anaemia, given the patient's age, the lack of history of exposure to cold, and the history which is given of antibiotic prescription.

### Question 41 of 206

Which of the following statements regarding disseminated intravascular coagulation (DIC) is most correct?

(Please select 1 option)

<input type="radio"/>	DIC is associated with a rising platelet count
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<input type="radio"/>	DIC is associated with an elevated D-dimer
<input type="radio"/>	DIC is associated with rising fibrinogen
<input type="radio"/>	Normal clotting parameters effectively exclude a diagnosis of DIC
<input type="radio"/>	Removal of the underlying cause of the DIC will lead to resolution of the manifestations of DIC
<input checked="" type="radio"/>	DIC is associated with an elevated D-dimer <b>This is the correct answer</b>

DIC is caused by the enhanced and abnormally sustained generation of thrombin and is associated with elevated products of fibrin breakdown, one of these being D-dimer.

Treatment of the underlying cause, for example, sepsis, does not always lead to resolution of the condition.

DIC is associated with a falling platelet count and decreased fibrinogen, but the clotting factors may be normal, especially when one considers that the acute phase response may shorten the activated partial thromboplastin time (APTT) and increase fibrinogen.

#### Question 42 of 206

In the consideration of disseminated intravascular coagulation (DIC), which of the following statements is most correct?

(Please select 1 option)

<input type="radio"/>	In DIC associated with sepsis secondary to retained products of conception, treatment of antibiotics will alleviate the process
<input type="radio"/>	Organ failure is a common finding in DIC

<input type="radio"/>	The intrinsic pathway is not involved in the pathophysiology of DIC
<input type="radio"/>	The presence of DIC does not increase mortality from the underlying disease
<input type="radio"/>	There are no randomised control trials to guide treatment in DIC

<input checked="" type="radio"/>	Organ failure is a common finding in DIC <b>This is the correct answer</b>
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DIC is caused by the enhanced and abnormally sustained generation of thrombin.

Organ failure is a common finding, being as common as bleeding in DIC, and is likely to be due to fibrin deposition within the organ.

The presence of DIC significantly increases mortality rates in affected patients, and treatment of the underlying cause of the DIC, for example, sepsis, does not always lead to resolution of the condition.

Secondary bursts of thrombin formation seen in DIC are instigated by the intrinsic pathway.

### Question 43 of 206

A 16-year-old girl with sickle cell disease presented with malaise and rapidly increasing dyspnoea.

A full blood count showed:

<b>Hb</b>	51 g/L	(115-165)
<b>Reticulocyte count</b>	$5.5 \times 10^9/L$	(25-85)

What is the most likely cause?

(Please select 1 option)

<input type="radio"/>	Epstein-Barr virus
<input type="radio"/>	Hepatitis E virus
<input type="radio"/>	Human immunodeficiency virus
<input type="radio"/>	Human papillomavirus-16 (HPV 16)
<input type="radio"/>	Parvovirus B19

<input checked="" type="radio"/>	Parvovirus B19 <b>This is the correct answer</b>
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Aplastic crisis in sickle cell anaemia (SSA) is caused by infection with the parvovirus B19.

The virus infects red cell progenitors in bone marrow, resulting in cessation of erythropoiesis and a very rapid drop in haemoglobin.

The condition is self-limited, with bone marrow recovery occurring in 7-10 days, followed by brisk reticulocytosis

#### Question 44 of 206

A 50-year-old female presents with acute chest pain and dyspnoea.

Examination reveals bilateral ankle oedema with 24-hour urine protein assessment showing 8 g/d (<0.2).

Which is the most likely explanation for these findings?

(Please select 1 option)

<input type="radio"/>	Factor V Leiden
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<input type="radio"/>	Reduced antithrombin III activity
<input type="radio"/>	Reduced concentration of von Willebrand's factor
<input type="radio"/>	Reduced factor VIII
<input type="radio"/>	Reduced fibrinogen concentration
<input checked="" type="radio"/>	Reduced antithrombin III activity <b>This is the correct answer</b>

This patient has developed nephrotic syndrome and appears to have had a thromboembolic event.

The suggestion is that she has had nephrotic syndrome before developing the thromboembolism.

Deranged coagulation associated with nephrotic syndrome is a consequence of AT III deficiency, increased fibrinogen and increased factor VIIIc.

### Question 45 of 206

Which of the following statements is most true regarding polycythaemia rubra vera (PRV)?

(Please select 1 option)

<input type="radio"/>	PRV is often associated with hypertension and smoking
<input type="radio"/>	PRV is usually associated with a high haemoglobin, but with neutropenia and thrombocytopenia
<input type="radio"/>	PRV may be characterised by a raised packed cell volume (PCV) and decreased plasma volume
<input type="radio"/>	The diagnosis of PRV can be made based on a high red cell mass,

	reduced EPO and characteristic bone marrow biopsy findings
<input type="radio"/>	Venesection treatment will improve long term survival rates
<input checked="" type="radio"/>	The diagnosis of PRV can be made based on a high red cell mass, reduced EPO and characteristic bone marrow biopsy findings <b>This is the correct answer</b>

The diagnosis of PRV is based on the revised WHO criteria. Diagnosis requires two major criteria and one minor criterion, or the first major criterion and two minor criteria.

Major criteria:

- Haemoglobin of more than 185 g/L in men, 165 g/L in women, or elevated red cell mass greater than 25% above mean normal predicted
- Presence of JAK 2 mutations, commonly 617V F

Minor criteria:

- Bone marrow biopsy showing hypercellularity with prominent erythroid, granulocytic and megakaryocytic proliferation
- Serum EPO below normal range
- Endogenous erythroid colony formation in vitro.

Oxygen saturations, splenic size, platelet count and white cell count no longer feature in the diagnostic criteria.

A decreased plasma volume causing a raised PCV is known as apparent or spurious polycythaemia. This may be associated with hypertension or smoking.

PRV is usually associated with a raised haemoglobin and often with a high platelet count and white cell count.

Venesection will lessen the rates of thrombotic complications but there is no evidence that venesection improves long-term survival rates.

### Question 46 of 206

A 30-year-old woman presents with jaundice and her investigations reveal:

<b>Haemoglobin</b>	90 g/L	(115-165)
<b>Reticulocyte count</b>	$180 \times 10^9/L$	(25-85)
<b>Serum bilirubin</b>	50 $\mu\text{mol/L}$	(1-22)

Her blood film reveals the presence of spherocytes.

Which of the following is the next most useful investigation?

(Please select 1 option)

<input type="radio"/>	Abdominal ultrasound scan
<input type="radio"/>	Direct antiglobulin test
<input type="radio"/>	Glucose-6-phosphate dehydrogenase activity
<input type="radio"/>	Haemoglobin electrophoresis
<input type="radio"/>	Red cell osmotic fragility
<input checked="" type="radio"/>	Direct antiglobulin test <b>This is the correct answer</b>

The results given indicate a haemolytic anaemia of which spherocytes are typical and given the age of the patient the most likely cause is immune.

The first step in analysis of a spherocytic hemolytic anaemia is to determine whether the process is hemolytic or not. The best way to do it is a direct antiglobulin test. If negative, one could go on to confirm HS with other tests.

The osmotic fragility test is unreliable and is no longer recommended in routine clinical practice. Osmotic gradient ektacytometry is used to differentiate hereditary spherocytosis from hereditary stomatocytosis, but is only available in specialised laboratories. If the diagnosis is equivocal, the cryohaemolysis test and EMA binding can be used.

In atypical cases, gel electrophoresis analysis of erythrocyte membranes is the test of choice.

**Question 47 of 206**

Exam Themes May 2002

A 35-year-old male with a long history of ulcerative colitis is treated for an acute exacerbation which settles following an alteration of his medication.

Six weeks after discharge he is re-admitted with sepsis and his results show:

<b>Haemoglobin</b>	105 g/L	(130-180)
<b>White cell count</b>	$2.0 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$90 \times 10^9/\text{L}$	(150-400)

Which one of the following drugs is most likely to be the cause of his pancytopenia?

(Please select 1 option)

<input type="radio"/>	Azathioprine
<input type="radio"/>	Mesalazine
<input type="radio"/>	Metronidazole
<input type="radio"/>	Pamidronate
<input type="radio"/>	Prednisolone

<input checked="" type="radio"/>	Azathioprine <b>This is the correct answer</b>
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Although both azathioprine and mesalazine cause pancytopenia, it is more commonly seen in patients undergoing azathioprine therapy.

Therefore this is 'most likely' to be the cause.

### Question 48 of 206

A 75-year-old woman receives two units of packed red cells following a hip replacement. One week later her haemoglobin concentration had fallen by 4 g/L.

Which one of the following would be most likely to indicate a delayed transfusion reaction?

(Please select 1 option)

<input type="radio"/>	Conjugated hyperbilirubinaemia
<input type="radio"/>	Elevated D dimer concentration
<input type="radio"/>	Haemoglobinuria
<input type="radio"/>	Haemosiderinuria
<input type="radio"/>	Positive direct antiglobulin test

<input checked="" type="radio"/>	Positive direct antiglobulin test <b>This is the correct answer</b>
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The features suggest immune haemolysis with direct antiglobulin test (DAT) being diagnostic.

Conjugated hyperbilirubinaemia is inappropriate as it is unconjugated bilirubin that is raised in haemolysis.

The remaining incorrect answers are not going to be diagnostic of an immune haemolytic transfusion reaction.

#### Question 49 of 206

A 71-year-old man presents with a tender left calf and has a background history of headaches, tiredness and dizziness. He is a smoker of 20 cigarettes daily and drinks 45 units of alcohol weekly.

On examination, he was plethoric, had a blood pressure of 186/102 mmHg and has a swollen, hot, tender, and erythematous left calf. Dopplers confirm the presence of a deep vein thrombosis.

Investigations reveal:

<b>Haemoglobin</b>	190 g/L	(130-180)
<b>Haematocrit</b>	0.58	(0.40-0.52)
<b>White cell count</b>	$12.5 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$500 \times 10^9/\text{L}$	(150-400)

Which one of the following is the most appropriate initial investigation to establish the diagnosis?

(Please select 1 option)

<input type="radio"/>	Abdominal ultrasound scan
<input type="radio"/>	Arterial blood gases
<input type="radio"/>	Bone marrow trephine
<input type="radio"/>	Leucocyte alkaline phosphatase score

<input type="radio"/>	Red blood cell mass
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<input checked="" type="radio"/>	Red blood cell mass <b>This is the correct answer</b>
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The most significant abnormality is the raised haemoglobin and haematocrit, suggesting polycythaemia. This can be either primary or secondary, and both are possibilities in this case. Smoking can result in secondary polycythaemia, but the raised white cell and platelet count are suspicious for a primary cause. Another possible cause is spurious polycythaemia which is caused by depleted plasma volume rather than raised red cell mass. Treatment of these conditions varies significantly and therefore it is important to distinguish between them.

Therefore, the most useful and appropriate initial investigation is red cell mass studies which will distinguish between true and relative polycythaemia.

Further investigations will then be dictated by the the results of this initial test; an ultrasound scan (USS) bone marrow, etc., and blood gases may be needed after the initial red cell mass studies. Whilst a bone marrow trephine is likely to be definitive in determining if a myeloproliferative disorder is present, it is invasive and therefore it is important to establish whether true polycythaemia is present first.

The leucocyte alkaline phosphatase score is rather outdated and seldom performed.

### Question 50 of 206

A 53-year-old woman presents with a six-month history of recurrent facial and tongue swelling.

She associated the attacks with consuming certain food additives and with contact with some cosmetics and cleaning fluids. Her only regular medication was hormone replacement therapy.

Investigations reveal:

<b>Total serum IgE</b>	145 kU/L	(0-120)
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<b>Serum C3</b>	105 mg/dL	(65-190)
<b>Serum C4</b>	35 mg/dL	(15-50)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	C1 esterase inhibitor deficiency
<input type="radio"/>	Chemical intolerance
<input type="radio"/>	Food allergy
<input type="radio"/>	Idiopathic angio-oedema
<input type="radio"/>	Mastocytosis
<input checked="" type="radio"/>	Food allergy <b>This is the correct answer</b>

The history suggests atopy which is confirmed by the mildly elevated IgE concentration and normal C4 and C3 concentrations.

Hereditary or acquired angio-oedema is unlikely given the normal C4 and the history occurs late. Also, the patient herself has noticed a link with food; food allergy is usually easier to diagnose in adults.

The cosmetics (chemical intolerance) are unlikely and the clinical history does not fit mastocytosis.

**Question 51 of 206**

A 30-year-old man presents with episodic jaundice and anaemia and has been diagnosed with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

On further testing, his wife has normal plasma G6PD activity.

Which one of the following statements is correct?

(Please select 1 option)

<input type="radio"/>	50% of their children will be affected, irrespective of gender
<input type="radio"/>	All of their children will be affected
<input type="radio"/>	All of their daughters will be affected
<input type="radio"/>	All of their sons will be affected
<input type="radio"/>	None of their children will be affected

<input checked="" type="radio"/>	None of their children will be affected <b>This is the correct answer</b>
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G6PD is X-linked, therefore females are carriers, and are not usually affected unless there is inactivation of their X chromosome. Males are affected.

Males will pass on the 'bad' X chromosome to their daughters so that they become carriers, and as said above they are not usually affected. Males pass on their Y chromosomes to any sons, therefore they will not be affected.

In the question, the male is affected, but as the female has normal levels of the enzyme, we are assuming she is not a carrier (although strictly she could be a carrier and have normal levels).

The male will pass on the X chromosome to any daughters, who will not be affected, as they will have a 'good' X from the mothers, and the father will pass on the Y chromosome to his sons, who will not be affected.

**Question 52 of 206**

A 62-year-old male is diagnosed with chronic myeloid leukaemia and his investigations show that both Philadelphia chromosome and bcr/abl gene is present.

What is the significance of the presence of the bcr/abl gene?

(Please select 1 option)

<input type="radio"/>	Acts on stem cell line DNA
<input type="radio"/>	Blocks apoptosis
<input type="radio"/>	Codes for the production of a tyrosine kinase in the leukaemic cells
<input type="radio"/>	Increases expression of granulocyte colony stimulating factor receptors on the cell membrane
<input type="radio"/>	Increases production of granulocyte colony stimulating factor

<input checked="" type="radio"/>	Codes for the production of a tyrosine kinase in the leukaemic cells <b>This is the correct answer</b>
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The product of the bcr/abl gene that is seen in 97% cases of chronic myeloid leukaemia is a constitutively active tyrosine kinase; this is responsible for the leukaemic process.

### Question 53 of 206

A 40-year-old man presents with bleeding gums and ease of bruising. His only medication is lansoprazole for dyspepsia.

Investigations show:

<b>Haemoglobin</b>	125 g/L	(130-180)
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<b>MCV</b>	90 fL	(80-96)
<b>Platelets</b>	$20 \times 10^9/L$	(150-400)
<b>Prothrombin time</b>	13.5 s	(11.5-15.5)

Blood film shows occasional giant platelets.

Which is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Amegakaryocytic thrombocytopenia
<input type="radio"/>	Disseminated intravascular coagulation
<input type="radio"/>	Drug-induced thrombocytopenia
<input type="radio"/>	Immune thrombocytopenic purpura
<input type="radio"/>	Thrombotic thrombocytopenic purpura
<input checked="" type="radio"/>	Immune thrombocytopenic purpura <b>This is the correct answer</b>

The only abnormality is the very low platelet count.

The bone marrow is still working as there are giant platelets seen on film, which you see when there is peripheral consumption of the platelets.

The large platelets are a sign that the bone marrow is churning them out prematurely to keep up with demand.

With disseminated intravascular coagulation, the prothrombin time would be prolonged.

A diagnosis of thrombotic thrombocytopenic purpura (TTP) requires the presence of microangiopathic haemolysis, thrombocytopenia, neurological abnormalities, fever and renal dysfunction.

Drug-induced thrombocytopenia occurs due to the induction of antibodies towards platelets. It differs from ITP in that the platelet destruction stops once the drug is withdrawn (c.f. ITP - continues despite drug withdrawal). While lansoprazole can cause a reduction in platelet count, it is not classically a drug you associate with drug-induced thrombocytopenia.

Immune thrombocytopenic purpura (ITP) results from antibody-mediated destruction of platelets. Most often the stimulus is unknown, but it can be secondary to other autoimmune disorders (e.g. SLE), viral infections (e.g. CMV, VZV, hepatitis C, HIV), *Helicobacter pylori*, medication and lymphoproliferative disorders. It results in isolated thrombocytopenia, with the most common presenting sign being a purpuric rash.

### Question 54 of 206

#### Core Questions

A 30-year-old female presents to the antenatal clinic with her first pregnancy.

During the interview, she reports that she has been entirely well but her sister had suffered a deep vein thrombosis in her second pregnancy. A thrombophilia screen shows that she is heterozygous for factor V Leiden (FVL).

Which is the most appropriate action for this patient?

(Please select 1 option)

<input type="radio"/>	She should be informed to seek medical attention if she becomes aware of calf swelling or pain
<input type="radio"/>	She should be treated with aspirin 75 mg daily
<input type="radio"/>	She should be treated with prophylactic low molecular weight heparin
<input type="radio"/>	She should be treated with prophylactic unfractionated heparin
<input type="radio"/>	She should receive warfarin

<input checked="" type="radio"/>	She should be informed to seek medical attention if she becomes aware of calf swelling or pain <b>Correct</b>
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Although she is heterozygous for factor V Leiden, she has not had a previous thrombotic event.

There is no need to anticoagulate her throughout pregnancy. However, she is at increased risk (pregnant and FVL) and should be very alert to the symptoms and signs of a thrombotic event.

There is no evidence of benefit from aspirin to reduce her thrombotic risk.

### Question 55 of 206

A 69-year-old male presents with tiredness and dyspnoea and is diagnosed with acute myeloid leukaemia.

Which of the following is the most important prognostic factor?

(Please select 1 option)

<input type="radio"/>	Elevated lactate dehydrogenase activity
<input type="radio"/>	Karyotype of bone marrow
<input type="radio"/>	Monocytic morphology
<input type="radio"/>	Number of blasts in bone marrow
<input type="radio"/>	White cell count at diagnosis

<input checked="" type="radio"/>	Karyotype of bone marrow <b>This is the correct answer</b>
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White cell count at diagnosis is important but most important is the karyotype of bone marrow, as this result stratifies patients into lower risk, standard risk, and poor risk, which has prognostic significance.

The remaining incorrect answers have no prognostic value.

### Question 56 of 206

A 72-year-old man presents with a five-day history of cough, dyspnoea and fever.

His chest x ray shows a left basal consolidation.

His full blood count shows:

<b>Haemoglobin</b>	110 g/L	(130-180)
<b>White cell count</b>	$30 \times 10^9/\text{L}$	(4-11)
<b>Neutrophils</b>	$10 \times 10^9/\text{L}$	(1.5-7)
<b>Lymphocytes</b>	$20 \times 10^9/\text{L}$	(1.5-4)
<b>Monocytes</b>	$1 \times 10^9/\text{L}$	(0-0.8)
<b>Eosinophils</b>	$0.4 \times 10^9/\text{L}$	(0.04-0.4)
<b>Basophils</b>	$0.1 \times 10^9/\text{L}$	(0-0.1)

Which one of the following is the most appropriate test to establish the diagnosis?

(Please select 1 option)

<input checked="" type="radio"/>	Bone marrow aspirate
<input type="radio"/>	Bone marrow cytogenetics

<input type="radio"/>	CT abdomen
<input type="radio"/>	Immunophenotyping of white cells
<input type="radio"/>	Sputum cytology and AFB

<input checked="" type="radio"/>	Immunophenotyping of white cells <b>Correct</b>
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Apart from the mild neutrophilia, which could be explained by the infection, the significant abnormality on the FBC is the lymphocyte count. Such a high lymphocyte count could be suggestive of a lymphoproliferative disorder such as chronic lymphocytic leukaemia. The best way to diagnose these is immunophenotyping of the blood: non-invasive and will give a diagnosis.

The patient may have lymphadenopathy or splenomegaly which would show on CT but no diagnosis can be made from this.

A bone marrow is invasive and the BM is sometimes not involved in low-grade lymphoproliferative disorders and, similarly, there may be no cytogenetic abnormality.

The FBC is not suggestive of TB or malignancy, therefore sputum examination would not be useful.

### Question 57 of 206

A 62-year-old male attends the Emergency Department with a severe nose bleed. He is known to have alcoholic cirrhosis.

His investigations reveal:

<b>Haemoglobin</b>	109 g/L	(130-180)
<b>White cell count</b>	$5 \times 10^9/L$	(4-11)

<b>Platelet count</b>	$60 \times 10^9/\text{L}$	(150-400)
<b>Prothrombin time</b>	17.5 s	(11.5-15.5)
<b>APPT</b>	42 s	(30-40)
<b>Fibrinogen</b>	0.7 g/L	(1.8-5.4)

What is the most appropriate blood product for this patient?

(Please select 1 option)

<input type="radio"/>	Cryoprecipitate
<input type="radio"/>	Factor VIII
<input type="radio"/>	Platelets
<input type="radio"/>	Prothrombin complex concentrate
<input type="radio"/>	Whole blood

<input checked="" type="radio"/>	Cryoprecipitate <b>Correct</b>
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The most significant abnormality is the low fibrinogen. Therefore the best product to correct the fibrinogen out of those given is cryoprecipitate.

To correct a coagulopathy you need to aim for:

- Fibrinogen  $>1.0 \text{ g/L}$
- Platelets  $>50 \times 10^9/\text{L}$

- PT and APTT <1.5 upper range of normal

From the results, you can see the most significant abnormality is the low fibrinogen.

The platelets are low and activated partial thromboplastin time/prothrombin time (APTT/PT) prolonged but not really sufficient to cause bleeding.

### Question 58 of 206

#### Core Questions

A 25-year-old female with a history of type 1 von Willebrand's disease (vWD) is referred for an opinion.

She is to have a cervical cone biopsy and the admitting team are concerned about her clotting.

You find that she has a past history of menorrhagia and has had two dental extractions as an adolescent that were uncomplicated.

Which is the most useful test to assess her bleeding tendency?

(Please select 1 option)

<input type="radio"/>	Activated partial thromboplastin time
<input type="radio"/>	Bleeding time
<input type="radio"/>	Plasma factor VIII activity
<input type="radio"/>	Platelet aggregation
<input type="radio"/>	Prothrombin time
<input checked="" type="radio"/>	Plasma factor VIII activity <b>This is the correct answer</b>

In type I vWD the prothrombin time (PT) and platelet aggregation will be normal.

Bleeding time, partial thromboplastin time (APTT) and factor VIII-coagulant (FVIIIc) are likely to be abnormal.

The bleeding time would be a good screening test but as we already know she has type I vWBD it will not give a quantitative measurement of her bleeding tendency.

Similarly, APTT will not be that useful.

The most useful test in practice is to do the vWB antigen and activity (RICO), but you would also do FVIIIc as this is also low in vWD.

### Question 59 of 206

A 75-year-old male is admitted with tiredness and lethargy and is found to have an enlarged right supraclavicular mass.

Past medical history reveals that he had developed acrocyanosis six months previously and two months ago, had been admitted with a chest infection for which he was treated with co-amoxiclav.

Investigations reveal:

- blood film red cell auto-agglutination
- direct antiglobulin test positive
- cold agglutinin test positive.

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Bronchial carcinoma
<input type="radio"/>	Drug-induced haemolysis
<input type="radio"/>	<i>Mycoplasma pneumoniae</i> infection
<input type="radio"/>	Non-Hodgkin's lymphoma (NHL)
<input type="radio"/>	Paroxysmal cold haemoglobinuria (PCH)
<input checked="" type="radio"/>	Non-Hodgkin's lymphoma (NHL) This is the correct answer

The results are consistent with an autoimmune haemolytic screen caused by a cold antibody. Drug-induced haemolysis does not give these results.

Bronchial Ca can give rise to an autoimmune haemolytic process but the antibody is usually warm; you do not get red cell agglutination or a positive cold agglutinin test.

PCH is a rare syndrome of acute intravascular haemolysis after exposure to cold caused by the Donath-Landsteiner antibody. It typically follows a viral illness or syphilis and is usually self-limiting.

The results and clinical description of acrocyanosis are consistent with a cold autoantibody (cold autoimmune haemolytic anaemia).

The antibody attaches to the RBCs in the peripheral circulation where the blood is cold, causing agglutination of the RBCs in the small vessels leading to the acrocyanosis.

It is an IgM Ab that can fix complement and cause both intra- and extravascular haemolysis. It can be a primary phenomenon (idiopathic cold haemagglutinin disease) or secondary to infection, for example, *Mycoplasma pneumoniae* or Epstein-Barr virus (EBV) or secondary to lymphoma.

The acrocyanosis developed before the chest infection, and in view of the lymphadenopathy, then NHL is the likely cause.

### Question 60 of 206

A 16-year-old girl presents with bilateral cervical lymphadenopathy. Her lymph node biopsy reveals a nodular sclerosing Hodgkin's disease.

Which one of the following features indicates a poorer prognosis?

(Please select 1 option)

<input type="radio"/>	Fatigue
<input type="radio"/>	Mediastinal mass of 3 cm
<input type="radio"/>	Night sweats
<input type="radio"/>	Pruritus

<input type="radio"/>	Recent Epstein-Barr virus infection
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<input checked="" type="radio"/>	Night sweats <b>Correct</b>
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Important prognostic features in Hodgkin's disease (HD) are stage B symptoms:

- fever
- night sweats, and
- weight loss.

A mass of >10 cm in size is also a poor prognostic factor.

Therefore although fatigue and pruritus are common, they have no prognostic significance.

EBV infection commonly is associated with HD but has no prognostic significance.

### Question 61 of 206

A 50-year-old woman with a long history of alcohol abuse is prescribed phenytoin for epilepsy.

Examination was normal except for a liver edge.

Her full blood count reveals:

<b>Haemoglobin</b>	100 g/L	(115-165)
<b>MCV</b>	122 fL	(80-96)
<b>White cell count</b>	$2.2 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$85 \times 10^9/\text{L}$	(150-400)

Which is the most likely explanation for these results?

(Please select 1 option)

<input type="radio"/>	Alcoholic liver disease
<input type="radio"/>	Aplastic anaemia
<input type="radio"/>	Folic acid deficiency
<input type="radio"/>	Hypothyroidism
<input type="radio"/>	Vitamin C deficiency

<input checked="" type="radio"/>	Folic acid deficiency <b>This is the correct answer</b>
----------------------------------	---

Folic acid deficiency would give all these results. In addition, she has good reason to be folate deficient since she drinks a considerable amount and is taking anticonvulsants.

Alcoholic liver disease on its own would not make her leucopenic.

Hypothyroidism would cause a raised MCV, but not the other parameters.

Scurvy does not cause this picture.

Aplastic anaemia could cause this haematological picture but the clinical scenario leads towards folic acid deficiency.

### Question 62 of 206

#### Core Questions

A 17-year-old male with glucose-6-phosphate dehydrogenase (G6PD) deficiency presents with tiredness and is noticed to be jaundiced. These features have developed since he developed a mild chest infection one week ago.

Which one of the following is the most likely finding?

(Please select 1 option)

<input type="radio"/>	Haemoglobinuria
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<input type="radio"/>	Low mean cell volume
<input type="radio"/>	Positive direct antiglobulin test
<input type="radio"/>	Reduced reticulocyte count
<input type="radio"/>	Spherocytes present on blood film

<input checked="" type="radio"/>	Haemoglobinuria <b>Correct</b>
----------------------------------	--------------------------------

G6PD deficiency is a red cell enzymopathy that can lead to acute intravascular haemolysis after exposure to certain drugs, infection, etc.

You would, therefore, get haemoglobinuria but would not get a positive direct antiglobulin test. The mean corpuscular volume (MCV) and reticulocyte count would be high due to haemolysis.

There is a form of G6PD deficiency where there is a chronic low-level haemolysis where there are spherocytes seen, but the clinical information points to intravascular haemolysis after an infection.

### Question 63 of 206

Concerning immune cell antigen receptors, which of the following statements is false?

(Please select 1 option)

<input type="radio"/>	Affinity maturation of the B cell receptor is an important process initiated during the primary immune response
<input type="radio"/>	IgD are surface receptors of B lymphocytes
<input type="radio"/>	In normal individuals T lymphocytes with T cell receptors (TCR) that recognise autoantigens are all deleted to prevent

	autoimmunity
<input type="radio"/>	TCRs with different antigen specificities can be co-expressed on a single T lymphocytes
<input type="radio"/>	The antigen specificity of the T cell receptor is generated during development

<input checked="" type="radio"/>	In normal individuals T lymphocytes with T cell receptors (TCR) that recognise autoantigens are all deleted to prevent autoimmunity <b>This is the correct answer</b>
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T and B lymphocytes express receptors on their surface that recognise antigen in a specific manner. Each individual lymphocyte expresses a single type of receptor with unique specificity (except dual specificity T cells - see below).

The receptor on the B lymphocyte is membrane bound immunoglobulin (IgM and IgD isotype) and recognises particulate antigen, whilst the TCR is a heterodimer that recognises peptide fragments presented by MHC molecules.

The antigen specificity of T and B cells is generated during development by recombination of gene segments encoding the variable domains (antigen recognition domains) of immune receptors. These gene recombinations are random and maturing lymphocytes that express autoreactive receptors which are then deleted or rendered anergic. These processes take place in the thymus (T lymphocytes) and in the bone marrow (B lymphocytes).

However, not all autoreactive lymphocytes are deleted during development. In the case of T lymphocytes, not all proteins are expressed in the thymus, and those that are present only in the periphery or at certain stages of development will encounter mature T cells that can respond to them. Thus, autoreactive T cells exist in the periphery and other mechanisms are responsible for the protection of the body against autoimmunity.

Affinity maturation refers to the process of progressive development of immunoglobulin with higher affinity to the antigen. This occurs in the germinal centres of lymphoid organs during the evolution of the humoral response and is accomplished by hypermutation of the variable

region genes. T cells with dual specificities have been reported although their function is unknown.

**Question 64 of 206**

Exam Themes May 2002

A 75-year-old male presents with a two-month history of dyspnoea, weight loss and generalised lethargy. His medical history included a previous left-sided hemiparesis due to stroke for which he took aspirin and perindopril.

Examination revealed residual left-sided hemiparesis together with a pale and slightly jaundiced appearance.

Investigations show:

<b>Haemoglobin</b>	50 g/L	(130-180)
<b>MCV</b>	109 fL	(80-96)
<b>White cell count</b>	$2 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$45 \times 10^9/\text{L}$	(150-400)

Urinalysis showed increased urobilinogen.

Which of the following is the next most appropriate investigation?

(Please select 1 option)

<input type="radio"/>	Bone marrow aspirate
<input type="radio"/>	Direct antiglobulin test
<input type="radio"/>	Endoscopy
<input type="radio"/>	Serum haptoglobins

<input type="radio"/>	Vitamin B <sub>12</sub> concentration
<input checked="" type="radio"/>	Vitamin B <sub>12</sub> concentration <b>This is the correct answer</b>

In this situation, serum B<sub>12</sub> estimation is the correct choice. With a pancytopenic picture and raised mean corpuscular volume (MCV), the most appropriate step is to check the B<sub>12</sub> and folate.

The other choices are considered only after the basic assays.

Haemolysis does not explain the low WCC, nor the thrombocytopenia.

A haptoglobin only adds weight to a diagnosis of haemolysis, and an RBC-labelled scan would add greater sensitivity to the diagnosis of haemolysis.

The mild jaundice is typical of megaloblastic anaemia (vitamin B<sub>12</sub> or folate deficiency) because of increased destruction of red cell precursors in the bone marrow.

### Question 65 of 206

A 55-year-old woman is referred by her GP with abnormal liver function tests.

She is overweight but otherwise well.

Liver biopsy is reported as showing evidence of non-alcoholic steatotic hepatitis (NASH).

Which of the following statements is correct concerning NASH?

(Please select 1 option)

<input type="radio"/>	Commoner in women than men
<input type="radio"/>	Has not shown improvement with pioglitazone
<input type="radio"/>	Is associated with insulin resistance
<input type="radio"/>	Is treated with urso-deoxycholic acid



The majority of patients will develop cirrhosis



Is associated with insulin resistance **This is the correct answer**

NASH is associated with increased prevalence of insulin resistance/type 2 diabetes.

Approximately 20% develop cirrhosis.<sup>1</sup>

It is more common in men due to the protective effects of oestrogen. The treatment is complex and multi-modal but should focus on weight reduction.

Data from small clinical trials using pioglitazone have shown modest improvement in liver biopsy appearance over one year.

### Question 66 of 206

A 52-year-old male presents with a history of lethargy and epistaxis over the last one month.

Examination reveals numerous bruises over arms and legs, splenomegaly and retinal haemorrhages.

A full blood count shows:

<b>Haemoglobin</b>	70 g/L	(130-180)
<b>White cell count</b>	$14 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$20 \times 10^9/\text{L}$	(150-400)

His blood film reveals white cells predominantly myeloblasts and promyelocytes.

Which one of the following investigations would be of most prognostic value?

(Please select 1 option)



Bone marrow aspiration

<input type="radio"/>	Bone marrow trephine biopsy
<input type="radio"/>	Cerebrospinal fluid examination
<input type="radio"/>	Cytogenetic karyotype
<input type="radio"/>	Immunophenotyping
<input checked="" type="radio"/>	Cytogenetic karyotype <b>This is the correct answer</b>

The history, full blood count results and the blood film are suggestive of acute myeloid leukaemia as there are numerous myeloblasts on film.

Of the answers given the cytogenetic karyotype is of most prognostic value.

The cytogenetic karyotype divides people into three categories:

- good risk
- standard risk, and
- poor risk.

### Question 67 of 206

A 56-year-old male was admitted for a total hip replacement due to osteoarthritis. There was no other medical history and physical examination was normal.

A routine pre-operative full blood count (FBC) showed:

<b>Haemoglobin</b>	110 g/L	(130-180)
<b>Platelet count</b>	$170 \times 10^9/\text{L}$	(150-400)
<b>White cell count</b>	$25 \times 10^9/\text{L}$	(4-11)

<b>Neutrophil count</b>	$5 \times 10^9/\text{L}$	(1.5-7)
<b>Lymphocyte count</b>	$19 \times 10^9/\text{L}$	(1.5-4)
<b>Monocyte count</b>	$0.9 \times 10^9/\text{L}$	(0-0.8)
<b>Eosinophil count</b>	$0.1 \times 10^9/\text{L}$	(0.04-4)
<b>Basophil count</b>	$0.08 \times 10^9/\text{L}$	(0-0.1)

His blood film shows mature lymphocytes.

What is the most appropriate initial management for this patient?

(Please select 1 option)

<input type="radio"/>	Cancel the patient's operation
<input type="radio"/>	Chlorambucil
<input type="radio"/>	Fludarabine
<input type="radio"/>	Observation
<input type="radio"/>	Prednisolone
<input checked="" type="radio"/>	Observation <b>This is the correct answer</b>

The most significant abnormality on the full blood count is the lymphocytosis, with mature lymphocytes seen on film.

In this age group, the most likely diagnosis is a low-grade lymphoproliferative disorder, for example, chronic lymphocytic leukaemia. This, as mentioned, is a low-grade condition, and does not require immediate treatment; patients undergo a period of observation, often quite lengthy, before any treatment is indicated.

The indication for treatment would include:

- disabling B symptoms
- lymphocyte doubling time of less than six months
- bone marrow compromise
- autoimmune haemolysis or immune thrombocytopenia.

He is never going to be cured of this condition, and therefore it would not be necessary to delay/cancel surgery. He may be slightly more at risk of infection, due to immune dysfunction that accompanies these conditions, and the surgeons should be aware of this.

### Question 68 of 206

A 17-year-old woman with non-Hodgkin's lymphoma underwent splenectomy for haemolytic anaemia.

She understood that she had an enhanced risk of developing overwhelming pneumococcal sepsis and wished to know how long this risk would persist.

What is the duration of the risk?

(Please select 1 option)

<input type="radio"/>	Up to 6 months
<input type="radio"/>	Up to 1 year
<input type="radio"/>	Up to 5 years
<input type="radio"/>	5 to 10 years
<input type="radio"/>	More than 10 years



More than 10 years **This is the correct answer**

The risk is thought to persist lifelong, and lifelong Penicillin prophylaxis is recommended.

### Question 69 of 206

#### Core Questions

A 70-year-old female presents with a three-month history of exertional dyspnoea and chest pain. She admitted to a poor diet, some vague abdominal pains and having lost 7 kg in weight.

Examination revealed pallor, patches of vitiligo on her arms and trunk, ankle oedema, and a palpable spleen.

Investigations revealed:

<b>Haemoglobin</b>	50 g/L	(115-165)
<b>MCV</b>	105 fL	(80-96)
<b>White cell count</b>	$2 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$50 \times 10^9/\text{L}$	(150-400)
<b>Bilirubin</b>	40 $\mu\text{mol/L}$	(1-22)
<b>ALT</b>	60 U/L	(1-31)
<b>AST</b>	40 U/L	(5-35)
<b>LDH</b>	1000 U/L	(10-250)

Which one of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Aplastic anaemia
<input type="radio"/>	Autoimmune haemolytic anaemia
<input type="radio"/>	Dietary folate deficiency
<input type="radio"/>	Pernicious anaemia
<input type="radio"/>	Sideroblastic anaemia

<input type="radio"/>	Pernicious anaemia <b>This is the correct answer</b>
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There is pancytopenia with anaemia being more significant. The anaemia is macrocytic.

Lactate dehydrogenase (LDH) is very high with some derangement of liver function tests (LFTs). Aplastic anaemia would cause pancytopenia but not a raised LDH.

Autoimmune haemolysis and sideroblastic anaemia would not cause pancytopenia.

Folate deficiency and pernicious anaemia would both cause the above results; the LDH is elevated due to ineffective erythropoiesis and likewise the deranged LFTs.

Pernicious anaemia is more likely given the history of other autoimmune disease.

Of note, with such a low haemoglobin one would expect a much higher mean corpuscular volume

(MCV); but sometimes when the deficiency is severe, the red cell anisopoikilocytosis causes a lower MCV.

### Question 70 of 206

A 73-year-old man presented with a two-week history of breathlessness and easy bruising.

Investigations show:

<b>Haemoglobin</b>	69 g/L	(130-180)
<b>White cell count</b>	$0.4 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$9 \times 10^9/\text{L}$	(150-400)

Bone marrow aspirate all cellular elements reduced.

Which drug is the most likely cause of these abnormalities?

(Please select 1 option)

<input type="radio"/>	Aciclovir
<input type="radio"/>	Amiloride
<input type="radio"/>	Amoxicillin
<input type="radio"/>	Paracetamol
<input type="radio"/>	Trimethoprim
<input checked="" type="radio"/>	Trimethoprim <b>Correct</b>

There is a pancytopenia and marrow aspirate shows reduction in production of all cellular elements.

Trimethoprim is the drug most likely of these five to cause depression of haematopoiesis, as this picture would be particularly unusual with paracetamol, amiloride, aciclovir and amoxicillin.

**Question 71 of 206**

A 28-year-old primigravid woman developed a swollen painful left leg at 12 weeks gestation. Doppler ultrasound of her leg venous system showed a left popliteal vein thrombosis.

Which one of the following treatments is associated with the greatest risk to the fetus?

(Please select 1 option)

<input type="radio"/>	Aspirin
<input type="radio"/>	Intravenous unfractionated heparin
<input type="radio"/>	Subcutaneous low molecular weight
<input type="radio"/>	Subcutaneous unfractionated heparin
<input type="radio"/>	Warfarin

<input type="radio"/>	Warfarin This is the correct answer
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Warfarin is generally avoided in pregnancy. In the first trimester, it is associated with an increased risk of miscarriage, and teratogenic side effects which include chondrodysplasia patellae, asplenia and diaphragmatic herniae. In the second and third trimesters, it is associated with retroplacental and intracerebral foetal haemorrhage, as well as foetal microcephaly, optic atrophy and developmental delay.

Low molecular weight heparin is the mainstay of treatment of veno-occlusive disease in pregnancy. It does not cross the placenta, but can be associated with maternal bone demineralisation and thrombocytopenia.

Aspirin appears to be relatively safe.

### Question 72 of 206

Exam Themes September 2004

A 61-year-old who has smoked for 40 years presents with thoracic back pain.

His investigations reveal:

<b>Haemoglobin</b>	111 g/L	(130-180)
<b>Urea</b>	9.3 mmol/L	(2.5-7.5)
<b>Creatinine</b>	298 µmol/L	(60-110)
<b>Calcium</b>	3.67 mmol/L	(2.2-2.6)
<b>Albumin</b>	30 g/L	(37-49)
<b>Total protein</b>	97 g/L	(61-76)
<b>Thoracic spine x ray</b>	Collapse of T8	

Which investigation would confirm the diagnosis?

(Please select 1 option)

<input type="radio"/>	Bone marrow aspirate
<input type="radio"/>	Creatinine clearance
<input type="radio"/>	CXR
<input type="radio"/>	ESR
<input type="radio"/>	PTH

<input checked="" type="radio"/>	Bone marrow aspirate <b>This is the correct answer</b>
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This man has myeloma. The smoking is a red herring.

Myeloma typically presents with back pain often associated with pathological fractures.

He is mildly anaemic, there is renal impairment and hypercalcaemia, with a raised total protein secondary to a paraproteinaemia.

Bone marrow examination would reveal increased plasma cells (greater than 4% and usually greater than 30%). The erythrocyte sedimentation rate will be raised, but the bone marrow aspirate would confirm the diagnosis irrefutably.

### Question 73 of 206

Exam Themes September 2004

A patient presents with acute promyelocytic leukaemia (APL).

Which of the following is the likely mechanism underlying leukaemogenesis?

(Please select 1 option)

<input type="radio"/>	Aberrant fusion of 2 genes
<input type="radio"/>	Impaired protein degradation
<input type="radio"/>	Over expression of cellular oncogene
<input type="radio"/>	Post-translational modification
<input type="radio"/>	Telomere shortening

<input checked="" type="radio"/>	Aberrant fusion of 2 genes <b>This is the correct answer</b>
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In APL, one of the retinoic acid receptor genes (RARA) is fused to PML in the great majority of patients as a result of the chromosomal translocation t(15; 17).

**Question 74 of 206**

Exam Themes September 2004

A patient with AML develops jaundice and spiking pyrexia three weeks into induction chemotherapy.

The patient remained pyrexial after seven days of intravenous antibiotics.

What is the likely diagnosis?

(Please select 1 option)

<input type="radio"/>	CMV
<input type="radio"/>	Fungal infection
<input type="radio"/>	Hepatic leukaemic deposits
<input type="radio"/>	Miliary TB
<input type="radio"/>	Toxoplasmosis

<input checked="" type="radio"/>	CMV This is the correct answer
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The most likely cause for the persisting pyrexia plus hepatitis in this immunocompromised patient treated with appropriate antibiotics would be a *Cytomegalovirus* infection.

Fungal infection would not be expected to cause the jaundice, but again may be responsible for the pyrexia.

TB would be most unlikely and hepatic infiltration would not be expected to produce this pyrexia.

**Question 75 of 206**

Which RBC antigen is involved in the entry of *P. vivax* into red blood cells?

(Please select 1 option)

<input type="radio"/>	Anti-D
<input type="radio"/>	Anti-S
<input type="radio"/>	Duffy
<input type="radio"/>	Kell
<input type="radio"/>	Kidd

<input checked="" type="radio"/>	Duffy This is the correct answer
----------------------------------	----------------------------------

The Duffy antigen receptor facilitates the entry of *P. vivax* into the red blood cells and Duffy negative individuals are therefore resistant to this strain.

A similar situation exists with *P. ovale* but Duffy negative offers slightly less protection.

### Question 76 of 206

Exam Themes September 2004

A 28-year-old pregnant woman is being treated for a deep vein thrombosis with unfractionated heparin.

A recent blood test shows:

<b>Haemoglobin</b>	98 g/L	(115-165)
<b>White cell count</b>	$9.5 \times 10^9/\text{L}$	(4-11)

<b>Platelets</b>	$35 \times 10^9/L$	(150-400)
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Which would be the best course of action for this woman?

(Please select 1 option)

<input checked="" type="radio"/>	Change to hirudin
<input type="radio"/>	Change to low molecular weight heparin
<input type="radio"/>	Change to warfarin
<input type="radio"/>	Danaparoid
<input type="radio"/>	No change in treatment and observe

<input checked="" type="radio"/>	Danaparoid <b>This is the correct answer</b>
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This patient appears to have [heparin-induced thrombocytopenia](#) (HIT). When HIT is suspected, heparin treatment should be discontinued and alternative anticoagulation should be started.

The heparinoid danaparoid appears to be the drug of choice for acute treatment and prophylaxis because of its low placental permeability.

Hirudin should only be used when either cross reactivity with heparin-induced antibodies, or cutaneous allergy against heparinoids are observed.

### Question 77 of 206

An 80-year-old man presents with tiredness and weakness.

A diagnosis of myelodysplastic syndrome is suspected.

Which of the following statements regarding myelodysplastic syndrome is correct?

(Please select 1 option)

<input type="radio"/>	Absence of ring sideroblasts on the blood film excludes myelodysplasia as a diagnosis
<input type="radio"/>	Cytotoxic chemotherapy is likely to be part of his treatment
<input type="radio"/>	He is more likely to die from an infection than from leukaemic transformation
<input type="radio"/>	If blast cells constitute 1% of the total white cells, this signifies leukaemic transformation
<input type="radio"/>	On a blood film, neutrophils typically show toxic granulation

<input checked="" type="radio"/>	He is more likely to die from an infection than from leukaemic transformation <b>Correct</b>
----------------------------------	--

The patient has myelodysplastic syndrome (MDS).

Myelodysplastic syndrome is a disease of old age. Men are affected more frequently than women. 80% of patients present because of symptoms of anaemia. The blood film typically shows pancytopenia with hypogranular neutrophils. The number of blasts seen varies.

The disease can be classified into the following subtypes( WHO classification 2008):

- Refractory anaemia with unilineage dysplasia- ie anaemia, neutropaenia or thrombocytopaenia (<5% blasts)
- Refractory anaemia with ring sideroblasts (<5% blasts; >15% sideroblasts)
- Refractory anaemia with multilineage dysplasia ( based on bone marrow dysplasia in 2 or more myeloid lineages)
- Refractory anaemia with excess blasts-1(5-9% blasts) and refractory anaemia with excess blasts -2 (10-19%)
- Myelodysplasia unclassified
- Myelodysplasia with isolated 5qdel( cytogenetic abnormality with prognostic significance)

Blasts > 20% is now classified as acute myeloid leukaemia.

Few patients require aggressive therapy and most need only supportive care. As the vast majority are elderly patients with other medical conditions, excessive intervention is unwarranted.

Transfusions of packed red cells or platelets may be required and antibiotics for intercurrent infections.

Granulocyte-colony stimulating factor (G-CSF) and recombinant erythropoietin (r-Epo) can improve blood counts. Aggressive cytotoxic chemotherapy is generally reserved for treatment of transformation to acute myelogenous leukaemia (AML) in younger patients.

Median survival is two years. Patients are more likely to have serious infections or life-threatening bleeds than blastic transformation.

### Question 78 of 206

Exam Themes September 2004

A 35-year-old lady with a history of two previous lower limb deep vein thromboses presents with a further DVT. She has a thrombophilia screen performed, which shows the presence of lupus anticoagulant.

What is the best course of action?

(Please select 1 option)

<input type="radio"/>	Aspirin
<input type="radio"/>	Aspirin and warfarin
<input type="radio"/>	Long-term low molecular weight heparin
<input type="radio"/>	Warfarin for six months
<input type="radio"/>	Warfarin lifelong
<input checked="" type="radio"/>	Warfarin lifelong <b>Correct</b>

This patient has recurrent DVTs and has been shown to have the presence of the lupus anticoagulant.

In the circumstances, evidence would suggest that lifelong anticoagulation with warfarin is required maintaining an international normalised ratio (INR) above 2.5.

### Question 79 of 206

A patient who received total body irradiation for the treatment of Hodgkin's lymphoma develops graft versus host disease (GVHD).

Which of the following blood products is likely to have caused this?

(Please select 1 option)

<input type="radio"/>	Cryoprecipitate
<input type="radio"/>	FFP
<input type="radio"/>	Frozen deglycerolised red blood cells
<input type="radio"/>	Immunoglobulin
<input type="radio"/>	Packed red blood cells
<input checked="" type="radio"/>	Packed red blood cells <b>This is the correct answer</b>

Graft versus host disease (GVHD) occurs when donor lymphocytes engraft in a susceptible recipient.

Products implicated in cases of transfusion associated (TA)-GVHD include:

- non-irradiated whole blood
- packed red blood cells
- platelets
- granulocytes, and
- fresh non-frozen plasma.

The following have not been implicated:

- frozen deglycerolised red blood cells
- fresh frozen plasma, and
- cryoprecipitate.

**Question 80 of 206**

Exam Themes May 2002

Which of the following is most likely to be reversible following venesection in a 45-year-old male with haemochromatosis?

(Please select 1 option)

<input type="radio"/>	Arthropathy
<input type="radio"/>	Cardiomyopathy
<input type="radio"/>	Cirrhosis
<input type="radio"/>	Diabetes mellitus
<input type="radio"/>	Hypopituitarism
<input checked="" type="radio"/>	Cardiomyopathy <b>This is the correct answer</b>

Disorders that are [potentially reversible in haemochromatosis](#) include the dermal pigmentation and cardiomyopathy.

Similarly, there are improvements in liver function tests.

However, diabetes, cirrhosis, hypogonadism, and arthropathy are usually irreversible.

**Question 81 of 206**

A 59-year-old male is referred with an abnormal full blood count (FBC).

He had presented to his general practitioner with a flu-like illness which has since subsided but a FBC revealed a platelet count of  $800 \times 10^9/L$  ( $150-400 \times 10^9$ ) which has remained persistently elevated but with no other abnormality on the FBC.

He is otherwise entirely asymptomatic and no abnormalities are noted on examination.

Which of the following is the most appropriate treatment for this patient?

(Please select 1 option)

<input type="radio"/>	Anagrelide
<input type="radio"/>	Aspirin
<input type="radio"/>	Hydroxycarbamide
<input type="radio"/>	Observation
<input type="radio"/>	Plateletpheresis

<input checked="" type="radio"/>	Observation <b>This is the correct answer</b>
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There are a number of adverse prognostic markers for essential thrombocythaemia (ET):

- Age above 60
- Symptomatology - particularly thrombosis and
- Platelet count above 1500.

Generally, the prognosis is extremely good in ET with survival of over two decades expected.

This patient would be regarded as low risk and hence observation only employed.

The risk of bleeding can also be a problem and although you may think that aspirin would be appropriate the evidence is conflicting.

### Question 82 of 206

What is the mechanism of action of low molecular weight heparin?

(Please select 1 option)

<input type="radio"/>	Activation of plasminogen
<input type="radio"/>	Chelation of calcium
<input type="radio"/>	Inhibition of activated factor X
<input type="radio"/>	Inhibition of antithrombin
<input type="radio"/>	Inhibition of vitamin K-dependent carboxylase

<input checked="" type="radio"/>	Inhibition of activated factor X <b>This is the correct answer</b>
----------------------------------	--

The shorter chain low molecular weight (LMW) fractions of heparin inhibit activated factor X but have less effect on thrombin (and on coagulation in general) than the high molecular weight (HMW) species.

### Question 83 of 206

If a patient with chronic renal failure is treated with erythropoietin (EPO), which of the following will be expected in this patient?

(Please select 1 option)

<input type="radio"/>	Decreased pure red cell aplasia
<input type="radio"/>	Decreased risk of hypertension
<input type="radio"/>	Decreased risk of thrombosis
<input type="radio"/>	Increased well being

<input type="radio"/>	Reduced appetite
<input type="radio"/>	Increased well being <b>This is the correct answer</b>

Increased viscosity is seen in EPO therapy which may exacerbate hypertension and there is also increased risk of thrombosis.

Pure red cell aplasia is a rare unwanted effect due to stimulation of antibodies by administered EPO which cross reacts with the patient's endogenous EPO.

Improvement in haemoglobin level results in the increased wellbeing and better appetite

#### Question 84 of 206

A 30-year-old male patient presents with sudden deterioration and haematuria, 15 minutes after starting blood transfusion.

His pulse rate is 120 beats per minute and blood pressure is 70/ 40 mmHg.

Which of the following is the most likely cause?

(Please select 1 option)

<input type="radio"/>	ABO incompatibility
<input type="radio"/>	Anaphylaxis to anaesthetic agents
<input type="radio"/>	Disseminated intravascular coagulation
<input type="radio"/>	Graft versus host disease
<input type="radio"/>	Rhesus incompatibility

<input checked="" type="radio"/>	ABO incompatibility <b>Correct</b>
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Immediate life-threatening reactions with intravascular haemolysis are caused by complement activating IgG or IgM antibodies.

They are usually ABO antibodies and these reactions can occur after transfusion of a few millilitres of blood.

### Question 85 of 206

A 55-year-old asymptomatic woman with mild splenomegaly was found to have a platelet count of  $650 \times 10^9/L$  (150-400) on blood investigation. White blood cells and haemoglobin are within the normal range.

What is the next step in management?

(Please select 1 option)

<input type="radio"/>	Anagrelide
<input type="radio"/>	Hydroxycarbamide
<input type="radio"/>	Low dose aspirin
<input type="radio"/>	Observation
<input type="radio"/>	Plateletpheresis

<input type="radio"/>	Observation <b>This is the correct answer</b>
-----------------------	---

In essential thrombocythosis low-risk patients have a risk of thrombosis similar to that of the age and sex-matched population and a very low risk of life-threatening bleeding, supporting close observation as the most sensible approach.

Hydroxycarbamide is an adequate choice for patients 60 years of age or older who are otherwise in good health.

For elderly patients with limited projected survival (less than 10 years) and who have problems with other drug compliance, 32P administration might be appropriate.

Anagrelide should be offered to younger patients (less than 60) who are at high risk by virtue of a prior history of thrombosis.

In patients who suffer from thrombotic episodes, especially episodes involving the microcirculation or large vessels, low-dose aspirin (100 mg/day) is usually administered.

In severe life-threatening episodes, rapid cytoreduction may be achieved by plateletpheresis or by the administration of a single dose of 0.4 mg/kg of nitrogen mustard.

### Question 86 of 206

A 23-year-old footballer was prescribed ibuprofen by his GP for a sprained ankle. Several hours later he felt very unwell and was passing dark urine.

The peripheral blood film shows many schistocytes.

The laboratory results show:

<b>Haemoglobin</b>	<90 g/L	(130-180)
<b>WBC</b>	$7 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$450 \times 10^9/\text{L}$	(150-400)
<b>Reticulocyte count</b>	5%	(0.5-2.4)
<b>Bilirubin</b>	40 mol/L	(1-22)

What is the most likely cause for his presentation?

(Please select 1 option)

<input type="radio"/>	Allergic reaction
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<input type="radio"/>	Autoimmune haemolytic anaemia
<input type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency
<input type="radio"/>	Paroxysmal nocturnal haemoglobinuria
<input type="radio"/>	Pyruvate kinase deficiency

<input checked="" type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency <b>This is the correct answer</b>
----------------------------------	--

This is a case of intravascular haemolysis with haemoglobinuria.

The patient has a history of taking ibuprofen which is an oxidant and causes haemolysis in patients with G-6-PD deficiency.

Oxidative stressors can be infectious agents, drugs, chemicals and certain legumes. In G-6-PD deficient patients, oxidative stress exposes interior sulfhydryl groups that are oxidised and cannot be reduced, leading to irreversible denaturation of the haemoglobin with Heinz body formation.

Schistocytes are red blood cell fragments that result from membrane damage. They are sometimes referred to as 'bite cells'.

### Question 87 of 206

Exam Themes September 2010

A 12-year-old boy was diagnosed with haemophilia A.

His uncle on his mother's side also has the same condition although his mother is well. The parents of the boy are worried about their next child suffering with the same condition.

What is the chance of the next child having the disease?

(Please select 1 option)

<input type="radio"/>	0%
<input type="radio"/>	25%
<input type="radio"/>	50%
<input type="radio"/>	75%
<input type="radio"/>	100%

<input checked="" type="radio"/>	25% <b>Correct</b>
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Haemophilia is an X-linked disease. In this scenario we are not told that the father has the disease, therefore, he must have a 'healthy' X chromosome. The mother's brother is affected - i.e. she is the carrier and has one affected X chromosome and one 'healthy'.

She will pass the affected chromosome to 50% of her daughters (meaning one in two will be a carrier) and 50% of her sons (meaning one in two will be affected by the disease) - i.e. one in four of her children will be affected by the disease, and one in four will be a carrier.

The sex of the next child it is not mentioned in this question. The overall chance of the next child having the disease will be 25% and phenotypically normal child will be 75%.

### Question 88 of 206

A 70-year-old male is diagnosed with multiple myeloma and is treated with melphalan and prednisolone.

Which of the following when added to this chemotherapeutic regime would be expected to improve survival?

(Please select 1 option)

<input type="radio"/>	Cyclosporin
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<input type="radio"/>	Interferon alpha
<input type="radio"/>	Methotrexate
<input type="radio"/>	Simvastatin
<input type="radio"/>	Thalidomide

<input checked="" type="radio"/>	Thalidomide <b>This is the correct answer</b>
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Significant improvements in survival may be expected through the addition of thalidomide to standard chemotherapeutic regimes.

Studies suggest a significant improvement at both two years and five years with thalidomide.

### Question 89 of 206

A 69-year-old man is seen in outpatients. He reports weight loss of 1 stone over three months but his history is otherwise unremarkable.

On examination, his abdomen is soft with no palpable masses. A PR examination is normal.

His blood tests show:

<b>Haemoglobin</b>	80 g/L	(120-160)
<b>MCV</b>	70 fL	(80-96)

Which of the following is the most appropriate investigation for this patient?

(Please select 1 option)

<input type="radio"/>	Abdominal x ray and colonoscopy
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<input type="radio"/>	CT scan of the abdomen and upper GI endoscopy
<input type="radio"/>	Sigmoidoscopy and upper GI endoscopy
<input type="radio"/>	Ultrasound scan of abdomen and colonoscopy
<input type="radio"/>	Upper GI endoscopy and colonoscopy
<input checked="" type="radio"/>	Upper GI endoscopy and colonoscopy <b>This is the correct answer</b>

This man has weight loss and an unexplained microcytic anaemia.

The likely site of blood loss is from the GI tract in absence of an alternative explanation.

This may be due to an occult GI malignancy and therefore the initial investigations of choice are upper and lower GI endoscopy.

### Question 90 of 206

A 78-year-old female who is on warfarin for atrial fibrillation presents with melaena.

Her blood pressure is 90/60 mmHg and heart rate is 100 bpm.

Investigations show:

<b>Haemoglobin</b>	90 g/L	(120-160)
<b>MCV</b>	87 fL	(83-95)
<b>INR</b>	7.2	(<1.4)

A PR examination confirms melaena.

Which is the best option for correcting the coagulopathy?

(Please select 1 option)

<input type="radio"/>	FFP
<input type="radio"/>	IV vitamin K
<input type="radio"/>	Stop warfarin
<input type="radio"/>	Stop warfarin and give IV vitamin K
<input type="radio"/>	Stop warfarin and give IV vitamin K and prothrombin complex concentrate

<input checked="" type="radio"/>	Stop warfarin and give IV vitamin K and prothrombin complex concentrate <b>This is the correct answer</b>
----------------------------------	---

This patient is hypotensive and tachycardic with melaena suggesting a major bleeding episode on warfarin. Treatment is based on the severity of bleeding independent of the INR.

In these circumstances, guidelines are: stop warfarin, give IV vitamin K (10 mg), and prothrombin complex concentrate (PCC) .

Local guidelines will be available in every NHS Trust. You must be familiar with these. If in doubt consult with the haematologist on call. FFP may not completely reverse the effects of warfarin so is not recommended in many local guidelines.

The rate of fatal haemorrhage in patients receiving warfarin approaches 1%.

### Question 91 of 206

A 50-year-old male who is well known to the Emergency Department attends inebriated.

He has an alcoholic encephalopathy with a Glasgow coma scale of 13. He is jaundiced, describes no symptoms, but is mildly short of breath.

You are presented with his blood results:

<b>Haemoglobin</b>	74 g/L	(120-160)
<b>White cell count</b>	$10.1 \times 10^9/\text{L}$	(4-10)
<b>Platelets</b>	$137 \times 10^9/\text{L}$	(140-400)
<b>Sodium</b>	133 mmol/L	(133-144)
<b>Potassium</b>	3.7 mmol/L	(3.5-4.9)
<b>Urea</b>	12 mmol/L	(2.5-7.5)
<b>Creatinine</b>	113 $\mu\text{mol/L}$	(60-110)
<b>AST</b>	124 U/L	(5-35)
<b>Alkaline Phosphatase</b>	224 U/L	(45-105)
<b>Total Protein</b>	54 g/L	(60-80)
<b>Bilirubin</b>	63 $\mu\text{mol/L}$	(1-22)
<b>Cholesterol</b>	15.3 mmol/L	(<5.5)
<b>Triglycerides</b>	7.2 mmol/L	(<2.2)
<b>Blood film</b>	Profound spherocytosis	

Which of the following is the most appropriate initial management for this patient?

(Please select 1 option)

<input type="radio"/>	IV steroids
<input type="radio"/>	MRI pancreas
<input type="radio"/>	Oesophagogastroduodenoscopy
<input type="radio"/>	Supportive therapy
<input type="radio"/>	Urgent laparotomy

<input checked="" type="radio"/>	Supportive therapy <b>This is the correct answer</b>
----------------------------------	--

A combination of jaundice, alcoholic hepatitis, hyperlipidaemia, and haemolysis is known as Zieve's syndrome.

There is no specific treatment for Zieve's syndrome but supportive therapy is indicated which includes:

- correction of clotting abnormalities
- treatment of haemolysis
- treating alcohol withdrawal
- preventing further alcohol intake, and
- adequate nutrition.

The spherocytosis is the result of the haemolysis.

Pancreatitis is a possible differential diagnosis here but in the first instance, one would request an amylase rather than an MRI of the pancreas.

### Question 92 of 206

Exam Themes September 2006

A 53-year-old male is receiving treatment with imatinib for chronic myeloid leukaemia.

Which of the following is imatinib?

(Please select 1 option)

<input type="radio"/>	Inhibits guanylate cyclase
<input type="radio"/>	Inhibits HER
<input type="radio"/>	Inhibits MAP kinase
<input type="radio"/>	Inhibits p53
<input type="radio"/>	Inhibits tyrosine kinase

<input checked="" type="radio"/>	Inhibits tyrosine kinase <b>Correct</b>
----------------------------------	---

Imatinib is an inhibitor of tyrosine kinase and is used in the treatment of conditions such as chronic myelocytic leukaemia (CML) and gastrointestinal stromal tumours (GIST).

It inhibits TK on abl proto-oncogene, c-kit and the PDGF-R.

In CML, the Philadelphia chromosome leads to a fusion protein of abl with bcr (breakpoint cluster region), termed bcr-abl. As this is now a continuously active tyrosine kinase, imatinib is used to decrease bcr-abl activity.

### Question 93 of 206

Exam Themes January 2007

A 22-year-old male presents with episodic nausea and abdominal pain although he has maintained a normal weight. The symptoms have been attributed to irritable bowel syndrome. There are no abnormalities on examination.

Blood tests were performed which reveal:

<b>Haemoglobin</b>	122 g/L	(130-180)
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<b>MCV</b>	92 fL	(80-96)
<b>White cell count</b>	$6.5 \times 10^9/L$	(4-11)
<b>Platelets</b>	$310 \times 10^9/L$	(150-400)
<b>Reticulocytes</b>	5%	(0.5-2.4)
<b>Bilirubin</b>	42 $\mu\text{mol/L}$	(1-22)
<b>AST/ALP</b>	Normal	
<b>Coombs' test</b>	Negative	
<b>Haptoglobin</b>	Mild decrease	

Which of the following is the likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute intermittent porphyria
<input type="radio"/>	Dubin-Johnson syndrome
<input type="radio"/>	Gilbert's syndrome
<input type="radio"/>	Hereditary spherocytosis
<input type="radio"/>	Viral hepatitis



Hereditary spherocytosis **This is the correct answer**

This patient has an elevated bilirubin concentration and elevated reticulocyte count suggesting haemolysis.

The most likely explanation would be hereditary spherocytosis which could be confirmed on blood film. This too explains the symptoms of nausea and abdominal pains suggesting gallstones, which are common even in mild disease.

Hereditary spherocytosis is usually an incidentally detected condition unless the person has active hemolysis, gall stones or uncomfortable splenomegaly. In this situation, which is not uncommon, the presentation is with gall stones. Haemolysis is predominantly extravascular, and haptoglobins are therefore only slightly decreased (rather than in intravascular haemolysis when they are more significantly depleted).

Gilbert's syndrome results in an isolated raised unconjugated bilirubin, whereas Dublin-Johnson syndrome is conjugated hyperbilirubinaemia.

Acute intermittent porphyria is due to a deficiency in haem production and results in episodes of severe abdominal pain usually associated with significant neurological symptoms.

You would expect raised ALT and AST in viral hepatitis.

#### Question 94 of 206

A 26-year-old man presents with dark urine, especially in the early morning. Further investigations show that he has haemoglobinuria and haemolytic anaemia.

A diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) is made.

Which of the following is the likely mechanism underlying this condition?

(Please select 1 option)



Aberrant fusion of two genes



Impaired protein degradation



Overexpression of cellular oncogene

<input type="radio"/>	Post-translational modification
<input type="radio"/>	Telomere shortening

<input checked="" type="radio"/>	Post-translational modification <b>This is the correct answer</b>
----------------------------------	---

Post-translational modification by the GPI glycolipid anchor is essential for the surface expression of many membrane proteins.

Defect of GPI biosynthesis due to somatic mutation in the haematopoietic stem cell is the basis for an acquired genetic disease, paroxysmal nocturnal haemoglobinuria.

The other mechanisms are associated with various other diseases.

### Question 95 of 206

A 24-year-old female student presented with fever and rigors for two days, fatigue, headache (especially retro-orbital), and diarrhoea. In particular she complained of a weakness of the left side of her face and drooping of the lip.

She had recently returned from a sabbatical in Uganda four weeks previously.

She was febrile (39.9°C), had a mild left facial nerve palsy, lymphadenopathy in her axillae and groin, and she had an erythematous, maculopapular rash.

Laboratory investigations showed:

<b>Haemoglobin</b>	120 g/L	(115-165)
<b>WBC</b>	$3.0 \times 10^9/L$	(4-11)
<b>Platelets</b>	$150 \times 10^9/L$	(150-400)
<b>Blood film</b>	Lymphopenia, some atypical lymphocytes seen	

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute HIV infection (seroconversion illness)
<input type="radio"/>	Dengue fever
<input type="radio"/>	Infectious mononucleosis
<input type="radio"/>	Typhoid fever
<input type="radio"/>	Viral hepatitis

<input checked="" type="radio"/>	Acute HIV infection (seroconversion illness) This is the correct answer
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Acute human immunodeficiency virus (HIV) seroconversion illness should be suspected where there has been a risk of exposure.

The symptoms and signs are often vague but the clinical presentation here is consistent. The median time from exposure to presentation is 25 days.

More than three-quarters of patients who become infected with HIV develop symptoms consistent with primary HIV infection.

Symptoms typically appear a few days to a few weeks after exposure to HIV, and generally include several of the following:

- Fever
- Rash, often erythematous maculopapular
- Fatigue
- Pharyngitis
- Generalised lymphadenopathy
- Urticaria
- Myalgia/arthralgia
- Anorexia
- Mucocutaneous ulceration

- Headache, retro-orbital pain
- Neurologic symptoms, e.g. aseptic meningitis, radiculitis, myelitis.

### Question 96 of 206

What is the mechanism of action of warfarin?

(Please select 1 option)

<input type="radio"/>	Activation of gamma-glutamyl carboxylase
<input type="radio"/>	Chelation of calcium
<input type="radio"/>	Inhibition of activated factor X
<input type="radio"/>	Inhibition of vitamin K-dependent carboxylase
<input type="radio"/>	Inhibition of vitamin K epoxide reductase
<input checked="" type="radio"/>	Inhibition of vitamin K epoxide reductase <b>This is the correct answer</b>

Warfarin inhibits epoxide reductase (specifically the VKORC1 subunit), thereby diminishing available vitamin K and vitamin K hydroquinone in the tissues which inhibit the carboxylation activity of the glutamyl carboxylase.

### Question 97 of 206

A 20-year-old man presented to hospital two days after returning from visiting his family in Bangladesh.

Within a day of his return to the United Kingdom, he suddenly developed profuse watery diarrhoea. He says there had been an outbreak of diarrhoea in his family's village in the week before his return.

Stool culture revealed a growth of *Vibrio cholerae*.

Which one of the following blood types is associated with the greatest susceptibility to severe cholera?

(Please select 1 option)

<input type="radio"/>	Blood Group A
<input type="radio"/>	Blood Group AB
<input type="radio"/>	Blood Group B
<input type="radio"/>	Blood Group O
<input type="radio"/>	Rhesus -ve

<input checked="" type="radio"/>	Blood Group O This is the correct answer
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Harris et al.<sup>1</sup> write that "Individuals with blood group O are more susceptible than other individuals to severe cholera, although the mechanism underlying this association is unknown."

### Question 98 of 206

#### Core Questions

A 16-year-old boy presents with a haemarthrosis that developed in his left knee following an injury in the garden.

His investigations show:

<b>Platelet count</b>	260 × 10 <sup>9</sup> /L	(150-400)
<b>Prothrombin time</b>	13 s	(11.5-15.5)

<b>Activated partial thromboplastin time</b>	80 s	(30-40)
<b>Factor VIII</b>	110 IU/dl	(50-150)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Antiphospholipid syndrome
<input type="radio"/>	Antithrombin III deficiency
<input type="radio"/>	Haemophilia A
<input type="radio"/>	Haemophilia B
<input type="radio"/>	von Willebrand's disease
<input checked="" type="radio"/>	Haemophilia B <b>This is the correct answer</b>

An elevated activated partial thromboplastin time (APTT) could be due to:

- Treatment with heparin
- Haemophilia
- von Willebrand's disease
- Antiphospholipid syndrome.

A normal factor VIII would suggest haemophilia B where there is lack of factor IX.

A prolonged APTT can be seen in von Willebrand's disease but factor VIII activity would be low.

The presentation is not consistent with antiphospholipid syndrome which is associated with thrombosis rather than haemorrhage. Antithrombin III deficiency is also associated with thrombosis and is most commonly acquired in the setting of nephrotic syndrome.

### Question 99 of 206

A 34-year-old Asian lady presented with tiredness and lethargy.

Her full blood count shows:

<b>Haemoglobin</b>	103 g/L	(115-165)
<b>Platelet count</b>	$320 \times 10^9/\text{L}$	(150-400)
<b>White cell count</b>	$10.6 \times 10^9/\text{L}$	(4-11)
<b>MCV</b>	68 fL	(80-96)
<b>HbA2</b>	5.2%	(2-3)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Beta-thalassaemia major
<input type="radio"/>	Beta-thalassaemia trait
<input type="radio"/>	Hereditary spherocytosis
<input type="radio"/>	Sickle cell disease



Beta-thalassaemia trait **This is the correct answer**

Microcytic anaemia would immediately raise the suspicion of iron deficiency perhaps from gastrointestinal or menstrual blood loss. However, the MCV here is disproportionately low. This combined with a raised HbA2 makes the diagnosis of beta-thalassaemia trait the most likely diagnosis.

"The diagnosis of beta thalassemia minor usually is suggested by the presence of an isolated, mild microcytic anemia, target cells on the peripheral blood smear, and a normal red blood cell count. An elevation of Hb A2 (2 alpha-globin chains complexed with 2 delta-globin chains) demonstrated by electrophoresis or column chromatography confirms the diagnosis of beta thalassemia trait. The Hb A2 level in these patients usually is approximately 4-6%. In rare cases of concurrent severe iron deficiency, the increased Hb A2 level may not be observed, although it becomes evident with iron repletion. The increased Hb A2 level also is not observed in patients with the rare delta-beta thalassemia trait."<sup>1</sup>

### Question 100 of 206

#### Core Questions

A 25-year-old man presents with an enlarged inguinal lymph node with night sweats. The most likely clinical diagnosis is Hodgkin's lymphoma.

An excision biopsy of the lymph node is performed.

Which one of the following findings on histopathology is associated with the best prognosis in Hodgkin's disease?

(Please select 1 option)

<input checked="" type="radio"/>	Lymphocyte depleted
<input type="radio"/>	Lymphocyte predominant
<input type="radio"/>	Mixed cellularity
<input type="radio"/>	Nodular sclerosing

<input type="radio"/>	Reed-Sternberg cells
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<input checked="" type="radio"/>	Lymphocyte predominant <b>This is the correct answer</b>
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Hodgkin's disease is characterised by Reed-Sternberg cells and this is, therefore, not a prognostic feature.

Nodular sclerosing is the most common finding and has a good prognosis.

Mixed cellularity also has a good prognosis.

Lymphocyte depleted has the worst prognosis.

The best prognosis is lymphocyte predominant.

### Question 101 of 206

Exam Themes May 2008

A 28-year-old man presented with recurrent nose bleeds and iron deficiency anaemia.

A chest x ray found a shadow over the right lung base and auscultation in this area revealed a bruit.

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Ehlers-Danlos syndrome
<input type="radio"/>	Hereditary haemorrhagic telangiectasia
<input type="radio"/>	Idiopathic thrombocytopenic purpura
<input type="radio"/>	von Willebrand's disease
<input type="radio"/>	Wegener's granulomatosis

<input checked="" type="radio"/>	Hereditary haemorrhagic telangiectasia <b>This is the correct answer</b>
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This is hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu syndrome) characterised by bleeding from telangiectasia on mucous membranes such as the nose, mouth and gastrointestinal tract.

Clinical examination reveals telangiectasia on the skin.

Arteriovenous malformation may be seen in the lung (as in this case) or brain.

### Question 102 of 206

A previously well 75-year-old woman presented with tiredness and a mildly raised lymphocyte count on her full blood count.

A blood film reports: "Smudge cells seen. Is this lady known to have chronic lymphocytic leukaemia?"

What is the most appropriate next investigation to confirm this woman's diagnosis?

(Please select 1 option)

<input type="radio"/>	Bone marrow aspirate
<input type="radio"/>	Bone marrow trephine
<input type="radio"/>	Immunophenotyping
<input type="radio"/>	Serum immunoglobulins
<input type="radio"/>	Ultrasound scan

<input checked="" type="radio"/>	Immunophenotyping <b>This is the correct answer</b>
----------------------------------	---

According to [Guidelines on](#) the diagnosis and management of chronic lymphocytic leukaemia, a definitive diagnosis of CLL is based on the combination of a lymphocytosis and characteristic lymphocyte morphology and immunophenotype.

The other tests are additional investigations all used in the workup of CLL.

### Question 103 of 206

A young woman presents with pallor, tiredness and fatigue.

Her full blood count is reported as typical of acute lymphoblastic leukaemia.

Which of the following is associated with the worst prognosis in ALL?

(Please select 1 option)

<input type="radio"/>	Female sex
<input checked="" type="radio"/>	Philadelphia chromosome present
<input type="radio"/>	Pre-B phenotype
<input type="radio"/>	Presentation in childhood
<input type="radio"/>	WCC of $21 \times 10^9/\text{L}$ at diagnosis

<input checked="" type="radio"/>	Philadelphia chromosome present <b>Correct</b>
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In acute lymphoblastic leukaemia:

Good prognostic factors:

- FAB L1 type
- Common ALL
- Pre-B phenotype
- Low initial WBC

Poor prognostic factors:

- FAB L3 type
- B, T cell type
- Philadelphia translocation, t(9;22)
- Increasing age at diagnosis
- Male sex
- CNS involvement
- High initial WBC (e.g. > 100).

### Question 104 of 206

A 14-year-old boy presents with excessive bleeding from a tooth cavity following an extraction at the dentist.

His investigations show:

<b>Haemoglobin</b>	132 g/L	(130-180)
<b>Platelet count</b>	$260 \times 10^9/\text{L}$	(150-400)
<b>White cell count</b>	$8 \times 10^9/\text{L}$	(4-11)
<b>Prothrombin time</b>	14 s	(11.5-15.5)
<b>Activated partial thromboplastin time</b>	45 s	(30-40)
<b>Factor VIII</b>	45 U/dL	(50-150)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Disseminated intravascular coagulation
<input type="radio"/>	Haemophilia A

<input type="radio"/>	Haemophilia B
<input type="radio"/>	Idiopathic thrombocytopenic purpura
<input type="radio"/>	von Willebrand's disease

<input checked="" type="radio"/>	von Willebrand's disease <b>This is the correct answer</b>
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This young boy with excessive bleeding has a slightly raised APTT and slightly reduced factor VIII. Whilst the amount of factor VIII present in haemophilia A can vary, you would expect it to be much less than described here (in severe haemophilia there is <1% of the normal level). In addition, the APTT is usually much more prolonged than described here.

In haemophilia B it is factor IX which is reduced. von Willebrand's disease is, therefore, the correct answer here. Factor VIII is slightly reduced as von Willebrand factor is a protective carrier for factor VIII.

DIC and ITP would typically be associated with thrombocytopenia.

### Question 105 of 206

A 56-year-old man is found to have a macrocytic anaemia with a megaloblastic bone marrow.

Which of the following causes of macrocytosis is the most likely cause?

(Please select 1 option)

<input type="radio"/>	Alcohol
<input type="radio"/>	Aplastic anaemia
<input type="radio"/>	Folate deficiency
<input type="radio"/>	Myelodysplasia

<input type="radio"/>	Reticulocytosis
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<input checked="" type="radio"/>	Folate deficiency <b>This is the correct answer</b>
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A megaloblastic bone marrow occurs in vitamin B<sub>12</sub> or folate deficiency and with some cytotoxic drugs.

The other causes of macrocytosis do not cause a megaloblastic bone marrow appearance.

### Question 106 of 206

A 65-year-old lady usually takes warfarin for a history of recurrent DVTs. Her warfarin is stopped and she is started on intravenous heparin prior to cardiac bypass for ischaemic heart disease.

She seems to require very high doses of heparin to achieve adequate anticoagulation, especially during surgery.

Which of the following conditions would explain her thrombophilia and her heparin resistance?

(Please select 1 option)

<input type="radio"/>	Activated protein C resistance
<input type="radio"/>	Antithrombin III deficiency
<input type="radio"/>	Lupus anticoagulant
<input type="radio"/>	Protein C deficiency
<input type="radio"/>	Protein S deficiency

<input checked="" type="radio"/>	Antithrombin III deficiency <b>This is the correct answer</b>
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Heparin resistance is seen in up to 22% of patients undergoing cardiopulmonary bypass surgery.

Several mechanisms resulting in heparin resistance have been identified, including antithrombin deficiency, increased heparin clearance, elevated heparin-binding proteins, and elevated factor VIII and fibrinogen levels.

For cardiopulmonary bypass in particular, rapid neutralisation of thrombin is required. In order for heparin to be successful in this, it requires antithrombin III which is an alpha2-globulin. It is therefore thought that antithrombin III deficiency is the underlying problem which is seen in patients resistant to heparin during cardiopulmonary bypass.

The other four answers describe conditions where there is an increased risk of thrombosis, but they are not specifically associated with resistance to heparin.

#### Question 107 of 206

A 60-year-old lady with bruising is investigated and found to have the following full blood count:

<b>Haemoglobin</b>	130 g/L	(115-165)
<b>White cell count</b>	$6.3 \times 10^9/\text{L}$	(4-11)
<b>Platelet count</b>	$15 \times 10^9/\text{L}$	(150-400)

She refuses to give consent to a bone marrow biopsy.

What is the most appropriate management plan?

(Please select 1 option)

<input type="radio"/>	Intravenous immunoglobulin
<input type="radio"/>	No treatment
<input type="radio"/>	Oral prednisolone

<input type="radio"/>	Platelet transfusion
<input type="radio"/>	Splenectomy

<input checked="" type="radio"/>	Oral prednisolone <b>This is the correct answer</b>
----------------------------------	---

This lady most likely has idiopathic thrombocytopenic purpura.

The history should highlight any drug causes (not mentioned here) and a blood film would help exclude leukaemia.

A bone marrow examination is useful, especially in the older person.

Platelet transfusion would not be helpful without treating the underlying cause.

No treatment is often an option but this lady is older and has bruising.

Given the circumstances, the best management plan is to treat with steroid.

### Question 108 of 206

Exam Themes January 2006

A 16-year-old boy with easy bruising and excessive bleeding from a tooth extraction is found to have von Willebrand's disease.

He is due to have further dental extractions and DDAVP is prescribed.

What is the mechanism of action of DDAVP in von Willebrand's disease?

(Please select 1 option)

<input type="radio"/>	Acts as a substitute carrier for factor VIII
<input type="radio"/>	Inhibits breakdown of von Willebrand's factor
<input type="radio"/>	Prevents renal excretion of von Willebrand's factor

<input type="radio"/>	Stimulates release of von Willebrand's factor from endothelial cells
<input type="radio"/>	Turns on the gene associated with von Willebrand's factor production

<input checked="" type="radio"/>	Stimulates release of von Willebrand's factor from endothelial cells <b>This is the correct answer</b>
----------------------------------	--

DDAVP may be given to increase the amount of the von Willebrand factor long enough for surgery or dental procedures to be performed.

DDAVP can provide a twofold to fivefold increase in plasma von Willebrand factor and factor VIII concentrations.

It induces cyclic adenosine monophosphate (cAMP)-mediated vWF secretion by a direct effect on endothelial cells.

### Question 109 of 206

Exam Themes January 2006

A 45-year-old man is diagnosed with acute promyelocytic leukaemia.

Which of the following chromosomal translocations is associated with this type of leukaemia?

(Please select 1 option)

<input type="radio"/>	t(8;9)
<input type="radio"/>	t(8;21)
<input type="radio"/>	t(9;22)
<input type="radio"/>	t(15;17)

<input type="radio"/>	t(17;22)
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<input checked="" type="radio"/>	t(15;17) This is the correct answer
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Acute promyelocytic leukaemia is characterised by a chromosomal translocation involving the retinoic acid receptor-alpha gene on chromosome 17 (RARA).

In 95% of cases, retinoic acid receptor-alpha (RARA) gene on chromosome 17 is involved in a reciprocal translocation with the promyelocytic leukaemia gene (PML) on chromosome 15.

### Question 110 of 206

Exam Themes January 2005

Burkitt's lymphoma is associated with a mutation of which of the following genes?

(Please select 1 option)

<input checked="" type="radio"/>	BCL-6 gene
<input type="radio"/>	BCR-ABL gene
<input type="radio"/>	Cyclin D1 gene
<input type="radio"/>	MYC gene This
<input type="radio"/>	RAR-alpha gene

<input checked="" type="radio"/>	MYC gene This is the correct answer
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Burkitt's lymphoma is a monoclonal proliferation of B lymphocytes, which results (in approximately 90% of the cases) from chromosome translocations that involve the Myc gene.

A chromosome translocation means that a chromosome is broken, which allows it to associate with parts of other chromosomes.

The classic chromosome translocation in Burkitt's lymphoma involves chromosome 8, the site of the MYC gene.

### Question 111 of 206

In idiopathic thrombocytopenic purpura, there are antibodies directed at which of the following?

(Please select 1 option)

<input type="radio"/>	ADP receptor
<input type="radio"/>	Antithrombin III
<input type="radio"/>	ATP receptor
<input type="radio"/>	Glycoprotein IIb/IIIa complex
<input type="radio"/>	Platelet-activating factor

<input checked="" type="radio"/>	Glycoprotein IIb/IIIa complex <b>Correct</b>
----------------------------------	--

In many cases of idiopathic thrombocytopenic purpura, the cause is not actually idiopathic but autoimmune, with antibodies against platelets being detected in approximately 80% of patients.

Most often these antibodies are against platelet membrane glycoproteins IIb-IIIa or Ib-IX, and are of the IgG type.

The coating of platelets with IgG renders them susceptible to opsonisation and phagocytosis by splenic macrophages.

### Question 112 of 206

Which of the following conditions would be expected to be associated with a raised leukocyte alkaline phosphatase (LAP) score?

(Please select 1 option)

<input type="radio"/>	Chronic myeloid leukaemia
<input type="radio"/>	Infectious mononucleosis
<input type="radio"/>	Myelofibrosis
<input type="radio"/>	Pernicious anaemia
<input type="radio"/>	Thrombocytopenic purpura

<input checked="" type="radio"/>	Myelofibrosis This is the correct answer
----------------------------------	--

The LAP score aids in the differential diagnosis of chronic myelocytic leukaemia (CML) versus leukaemoid reaction.

It also aids in the evaluation of:

- Polycythaemia vera
- Myelofibrosis with myeloid metaplasia, and
- Paroxysmal nocturnal haemoglobinuria.

Low scores have been associated with:

- CML
- Paroxysmal nocturnal haemoglobinuria (PNH)
- Thrombocytopenic purpura, and
- Hereditary hypophosphatasia.

High scores have been seen in:

- Polycythaemia vera
- Myelofibrosis

- Aplastic anaemia
- Multiple myeloma
- Down's syndrome (trisomy 21)
- Hodgkin's disease
- Lymphoma
- Hairy cell leukaemia
- Chronic and acute lymphatic leukaemia
- Pregnancy and immediately postpartum
- Leukaemoid reactions and
- Neutrophilia either physiological or secondary to infection.

It is classically normal in infectious mononucleosis, reactive polycythaemia and viral hepatitis.

### Question 113 of 206

Exam Themes January 2005

A 48-year-old woman with a history of epilepsy and ischaemic heart disease presented with the following full blood count.

<b>Haemoglobin</b>	74 g/L	(115 - 165)
<b>Mean cell volume</b>	125 fL	(80 - 96)
<b>White cell count</b>	$2.5 \times 10^9/\text{L}$	(4 - 11)
<b>Platelet count</b>	$130 \times 10^9/\text{L}$	(150 - 400)

Which of the following medications is the most likely cause?

(Please select 1 option)

<input type="radio"/>	Carbamazepine
<input type="radio"/>	Clopidogrel
<input type="radio"/>	Furosemide

<input type="radio"/>	Phenytoin
<input type="radio"/>	Spiroinolactone

<input checked="" type="radio"/>	Phenytoin <b>Correct</b>
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There is a macrocytic anaemia with low platelets and WCC typical of a nutritional deficiency.

Phenytoin can lead to folate deficiency and is, therefore, the most likely cause.

#### Question 114 of 206

A 40-year-old lady presents with a swollen right calf. She has a history of mental health problems and is on a number of medications.

Which of the following treatments increases the risk of thromboembolism?

(Please select 1 option)

<input type="radio"/>	Antipsychotics
<input type="radio"/>	Benzodiazepines
<input type="radio"/>	Monoamine oxidase inhibitors
<input type="radio"/>	Selective serotonin reuptake inhibitors
<input type="radio"/>	Tricyclic antidepressants

<input checked="" type="radio"/>	Antipsychotics <b>This is the correct answer</b>
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The oral contraceptive and antipsychotics are possible causes of thromboembolism.

**Question 115 of 206**

Exam Themes May 2006

A 70-year-old woman is on multiple medications for various conditions and she is found to have a macrocytic anaemia with a low serum B<sub>12</sub>.

Which of the following medications is a possible cause of the B<sub>12</sub> deficiency?

(Please select 1 option)

<input type="radio"/>	Amiodarone
<input type="radio"/>	Ezetimibe
<input type="radio"/>	Metformin
<input type="radio"/>	Nicotinic acid
<input type="radio"/>	Sodium valproate

<input checked="" type="radio"/>	Metformin This is the correct answer
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Long-term treatment with metformin increases the risk of vitamin B<sub>12</sub> deficiency. The possibility of metformin-associated B<sub>12</sub> deficiency should be considered in patients on metformin who suffer cognitive impairment, peripheral neuropathy, subacute combined degeneration of the cord or anaemia. Regular measurement of vitamin B<sub>12</sub> concentrations during long-term metformin treatment should be strongly considered.

Amiodarone may cause haemolytic anaemia, aplastic anaemia or thrombocytopenia but not B<sub>12</sub> deficiency.

Ezetimibe can cause thrombocytopenia but not B<sub>12</sub> deficiency.

Nicotinic acid can cause prolonged prothrombin time, and reduced platelet count but not B<sub>12</sub> deficiency.

Sodium valproate can cause blood disorders (including anaemia, leucopenia, pancytopenia) but not B<sub>12</sub> deficiency.

### Question 116 of 206

A 60-year-old Chinese man has been started by his general practitioner on quinine for leg cramps.

He presents a week later with five days of darkened urine and two days of increasing breathlessness, back pain, and fatigue.

Investigations show a haemoglobin of 70 g/L (130-180) and raised reticulocyte count.

Which of the following best explains this drug reaction?

(Please select 1 option)

<input type="radio"/>	Autoimmune haemolytic anaemia
<input type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency
<input type="radio"/>	Hereditary spherocytosis
<input type="radio"/>	Pyruvate kinase deficiency
<input type="radio"/>	Sickle cell disease

<input checked="" type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency <b>This is the correct answer</b>
----------------------------------	--

G6PDH (X-linked recessive) is seen in people of African, Mediterranean, Iraqi, Jewish, South East Asian, and Chinese origin, and predisposes to a haemolytic anaemia reaction with drugs or infection.

Implicated drugs include:

- aspirin
- sulphonamides
- antimalarials, and
- quinine/quinidine.

The haemolytic anaemia is non-immune (direct antiglobulin test [DAT] negative).

Pyruvate kinase deficiency is autosomal recessive and presents as a chronic haemolytic anaemia exacerbated by viral infections.

Hereditary spherocytosis is characterised by variable chronic non-immune haemolysis, exacerbated by infections.

### Question 117 of 206

A 44-year-old woman with type 1 diabetes mellitus has not attended the diabetic clinic for five years.

Examination shows no abnormalities.

Investigations show:

<b>Haemoglobin</b>	90 g/L	(115-165)
<b>MCV</b>	94 fL	(80-96)
<b>Haematocrit</b>	28%	-
<b>HbA<sub>1c</sub></b>	87 mmol/mol	(20-42)
	10.1%	(3.8-6.4)

A blood smear shows normochromic, normocytic anaemia.

Which of the following is the most likely cause?

(Please select 1 option)

<input type="radio"/>	Acute blood loss
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<input type="radio"/>	Chronic lymphocytic leukaemia (CLL)
<input type="radio"/>	Erythropoietin deficiency
<input type="radio"/>	Microangiopathic haemolysis
<input type="radio"/>	Sideroblastic anaemia

<input checked="" type="radio"/>	Erythropoietin deficiency <b>This is the correct answer</b>
----------------------------------	---

The most likely cause is progressive renal failure which leads to reduced release of erythropoietin from the kidneys.

Sideroblastic anaemia (myelodysplasia) is seen in older age groups.

CLL or microangiopathic haemolysis are possible causes but unlikely.

### Question 118 of 206

Which of the following statements regarding thrombocytosis is correct?

(Please select 1 option)

<input type="radio"/>	Erythropoietin is the key hormone in the regulation of megakaryocyte differentiation
<input type="radio"/>	May occur as a response to exercise
<input type="radio"/>	Occurs exclusively in essential thrombocythaemia
<input type="radio"/>	Secondary thrombocytosis is an indication for hydroxyurea therapy

<input type="radio"/>	The most common cause is essential thrombocythaemia
<input checked="" type="radio"/>	May occur as a response to exercise <b>This is the correct answer</b>

The most common cause of thrombocytosis is a reactive thrombocytosis.

Thrombocythaemia may occur in any of the myeloproliferative disorders, particularly polycythaemia rubra vera (PRV).

Thrombopoietin is the key hormone in the regulation of megakaryocyte differentiation.

Secondary thrombocytosis does not place the patient at risk for haemostatic or cardiovascular events.

### Question 119 of 206

Which of the following statements concerning abnormalities of the haemoglobin molecule is true?

(Please select 1 option)

<input type="radio"/>	Alpha thalassaemia is due to a deficiency of beta-chain production
<input type="radio"/>	Genes for the alpha and beta chains are located on the same chromosome
<input type="radio"/>	HbS is caused by a single base mutation on the beta-chain
<input type="radio"/>	In thalassaemia, persistence of HbF is an adverse prognostic sign
<input type="radio"/>	Oligonucleotide probes may assist in the diagnosis of haemoglobinopathies in adolescents

<input checked="" type="radio"/>	HbS is caused by a single base mutation on the beta-chain <b>This is the correct answer</b>
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Alpha thalassaemia is due to abnormalities of the alpha chain. Persistence of HbF has survival advantages in severely affected subjects.

Alpha is located on 16, beta on 11.

Hb electrophoresis is used in the adult, rather than oligonucleotide probes as used in the fetus.

### Question 120 of 206

Which of the following haematological disorders is inherited as an autosomal recessive condition?

(Please select 1 option)

<input type="radio"/>	Acute intermittent porphyria
<input type="radio"/>	Antithrombin III deficiency
<input type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency
<input type="radio"/>	Protein C deficiency
<input type="radio"/>	Pyruvate kinase deficiency

<input checked="" type="radio"/>	Pyruvate kinase deficiency <b>This is the correct answer</b>
----------------------------------	--

Acute intermittent porphyria is an autosomal dominant disorder resulting from partial porphobilinogen deaminase deficiency in the cytosol of all tissues including erythrocytes. Clinical expression of the disease is linked to environmental or acquired factors such as:

- nutritional status

- drugs
- steroids, and
- chemicals.

The major abnormality is of the peripheral, autonomic, or central nervous system (CNS).

Major symptoms are abdominal pain, nausea, vomiting, constipation, or diarrhoea. In severe cases, the urine develops a port wine colour due to the high content of porphobilin, an auto-oxidation product of PBG.

Hypertension and neuropathy are common, with muscle weakness, cranial nerve abnormality, and seizures.

Antithrombin III (AT3) is a plasma inhibitor protein that blocks the enzymatic activity of some serine proteases coagulation factors. The activity of this inhibitor is increased by heparin.

AT3 is synthesised by the liver, is not vitamin K-dependent, and can be consumed during disseminated intravascular coagulation (DIC). Normal newborns have a reduced activity. Congenital AT3 deficiency is autosomal dominant. Treatment of thrombotic events in these patients may be difficult.

Glucose-6-phosphate dehydrogenase deficiency is the most important disease of the pentose phosphate pathway, and is responsible for two clinical syndromes:

- an episodic haemolytic anaemia induced by infections or certain drugs, and
- a spontaneous chronic non-spherocytic haemolytic anaemia.

The deficiency is X-linked, and heterozygous females are resistant to falciparum infections. There are a large number of abnormal alleles causing disease of vastly different severity.

Protein C is an inhibitor that, once activated, inhibits clot formation and enhances fibrinolysis. It is liver synthesised and vitamin K-dependent. Protein C is converted to an active enzyme by a thrombin-thrombomodulin complex on the endothelial cell surface.

Activated protein C inhibits a plasminogen activator inhibitor, which results in enhanced fibrinolysis, and, with protein S as a co-factor, inhibits the clotting of the activated factors 5 and 8 by limited proteolysis. Activated protein C thus controls the conversion of factor 10 to 10a and prothrombin to thrombin.

Congenital deficiency is an autosomal dominant trait. Acquired deficiency may occur in association with infection.

Pyruvate kinase deficiency is a rare congenital haemolytic anaemia inherited as an autosomal recessive. Generation of adenosine triphosphate (ATP) within the red cell is impaired,

resulting in an abnormally high concentration of 2,3,DPG in the red cell, which inhibits the enzymes of the pentose phosphate pathway.

Clinical manifestations vary from severe neonatal haemolysis to a mild, well compensated haemolysis first noted in adulthood.

### Question 121 of 206

You are asked to provide advice on a 35-year-old woman who is admitted under the maxillo-facial surgeons for extraction of wisdom teeth.

The only concern was that she had developed prolonged bleeding following a tooth extraction 10 years previously and had required suturing. Besides this, she gave no other history of bleeding.

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Factor V Leiden
<input type="radio"/>	Factor IX deficiency
<input type="radio"/>	Factor XII deficiency
<input type="radio"/>	Primary antiphospholipid syndrome
<input type="radio"/>	von Willebrand's disease

<input checked="" type="radio"/>	von Willebrand's disease <b>This is the correct answer</b>
----------------------------------	--

Not that much is given away by this history, just the issue of a prolonged bleed after prior dental extraction.

The most likely diagnosis when considering this patient is von Willebrand's disease which is an autosomal dominant condition and is one of the commonest bleeding disorders. Most cases are mild, with bleeding after only mild injury, particularly mucosal membrane injuries.

The condition is due to a reduction or structural abnormality of von Willebrand's factor, which has the dual role of promoting normal platelet function and stabilising coagulation factor VIII.

von Willebrand's disease can give normal results on screening tests and diagnosis may require specialist investigation.

Most patients with mild disease respond to desmopressin (DDAVP) but clotting factor concentrates are needed for a minority.

### Question 122 of 206

A 17-year-old girl who had completed treatment for acute lymphoblastic leukaemia six months previously presents with a short history of marked right hip pain and associated limp.

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Avascular necrosis of the femoral head
<input type="radio"/>	Gout
<input type="radio"/>	Osteoarthritis
<input type="radio"/>	Pseudogout
<input type="radio"/>	Septic arthritis

<input checked="" type="radio"/>	Avascular necrosis of the femoral head <b>Correct</b>
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Avascular necrosis of the femoral head can occur as a consequence of her treatment or the disorder itself.

At age 17, osteoarthritis is particularly unlikely.

Gout too is unlikely (considering she completed treatment six months ago) unless she had relapsed (high white cell count) or had some other risk factors.

She would be considered to be no more likely to get septic arthritis or pseudogout than anyone who had not previously had acute lymphoblastic leukaemia, if in remission.

### Question 123 of 206

A 17-year-old girl with mild von Willebrand's disease is scheduled for dental extraction.

A previous dental extraction resulted in bleeding that had required two unit transfusion.

What is the most appropriate treatment prior to dental surgery?

(Please select 1 option)

<input type="radio"/>	Cryoprecipitate
<input type="radio"/>	DDAVP
<input type="radio"/>	Fresh frozen plasma
<input type="radio"/>	High purity factor VIII concentrate
<input type="radio"/>	Recombinant factor VIII concentrate

<input checked="" type="radio"/>	DDAVP This is the correct answer
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DDAVP (desmopressin) is the choice treatment for mild von Willebrand's disease, which would include type I, and the majority of type II, although there is some controversy in type II B as it is thought that DDAVP can exacerbate thrombocytopenia that can accompany this type of von Willebrand's.

It is of no use in type III - severe von Willebrand's disease. The history tells us that she has mild disease.

You would not use cryoprecipitate or fresh frozen plasma in these patients in this era due to potential viral transmission risk from blood products.

For severe disease, you would use a von Willebrand factor concentrate, not factor VIII concentrate.

### Question 124 of 206

An 18-year-old male presented with excessive bleeding following a tooth extraction.

His investigations showed:

<b>Platelet count</b>	$260 \times 10^9/L$	(150-400)
<b>Prothrombin time</b>	13 s	(11.5-15.5)
<b>Activated partial thromboplastin time</b>	86 s	(30-40)
<b>Factor VIII</b>	110 IU/dL	(50-150)

Deficiency of which of the following clotting factors is the most likely explanation for this patient?

(Please select 1 option)

<input type="radio"/>	II
<input type="radio"/>	V
<input type="radio"/>	VII
<input type="radio"/>	IX
<input type="radio"/>	X



**IX** This is the correct answer

An elevated APTT could be due to:

- treatment with heparin
- haemophilia
- von Willebrand's disease, or
- antiphospholipid syndrome.

A normal factor VIII would suggest haemophilia B where there is a lack of factor IX.

A prolonged APTT can be seen in von Willebrand's disease, but factor VIII activity would be low.

The presentation is not consistent with antiphospholipid syndrome and would also, typically, be associated with thrombocytopenia.

### Question 125 of 206

A 72-year-old man presents to the haematology clinic. He has suffered increasing headaches over the past few weeks, and unfortunately suffered a myocardial infarction some four weeks ago. He has been buying anti-histamines over the counter because of increasing itching.

During his admission it was noted that he had a marked elevation in haemoglobin, white cells and platelets. He is a non-smoker with no history of chest disease.

On examination in the clinic today he is hypertensive with a BP of 155/90 mmHg. Heart sounds are normal and his chest is clear. He looks plethoric with a ruddy complexion, and you notice that he has splenomegaly on abdominal examination.

Investigations show

<b>Haemoglobin</b>	198 g/L	(135-180)
<b>White cell count</b>	$18.7 \times 10^9/\text{L}$	(4-10)
<b>Platelets</b>	$672 \times 10^9/\text{L}$	(150-400)

<b>Sodium</b>	139 mmol/L	(134-143)
<b>Potassium</b>	4.7 mmol/L	(3.5-5)
<b>Creatinine</b>	140 µmol/L	(60-120)

Which of the following is the most likely mutation that he carries?

(Please select 1 option)

<input type="radio"/>	Bcr-abl
<input type="radio"/>	HER-1
<input type="radio"/>	HER-2
<input type="radio"/>	JAK 1
<input type="radio"/>	JAK 2
<input checked="" type="radio"/>	JAK 2 This is the correct answer

JAK2 V617F is detectable in 95% of patients with primary polycythaemia. It is a cytoplasmic tyrosine kinase which is responsible for signal transduction of haemopoietic growth factors, including erythropoietin.

JAK2 mutation is a primary event in the development of primary polycythaemia, with homozygosity for the mutation conferring a proliferative advantage for the cells concerned.

Currently, a new range of agents targeted against JAK2 is under development for the treatment of myeloproliferative disorders.

### Question 126 of 206

A 74-year-old man is being managed at the haematology/oncology clinic for suspected myeloma. He complains of symptoms of increasing shortness of breath over the past few weeks, with increased lethargy, decreased exercise tolerance, and increasing lower limb oedema.

On examination he looks pale, his BP is 139/81 mmHg, pulse 89. His heart sounds are normal, but there are bilateral crackles on auscultation of the chest and he has pitting lower limb oedema.

Investigations show:

<b>Haemoglobin</b>	102 g/L	(135-180)
<b>White cell count</b>	$8.7 \times 10^9/\text{L}$	(4-10)
<b>Platelets</b>	$185 \times 10^9/\text{L}$	(150-400)
<b>Sodium</b>	140 mmol/L	(134-143)
<b>Potassium</b>	4.3 mmol/L	(3.5-5)
<b>Creatinine</b>	135 $\mu\text{mol/L}$	(60-120)
<b>Albumin</b>	22 g/L	(35-50)
<b>Urine</b>	Protein +++	

What is the most likely cause of his underlying proteinuria?

(Please select 1 option)

<input type="radio"/>	AA amyloidosis
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<input type="radio"/>	AL amyloidosis
<input type="radio"/>	BPP amyloidosis
<input type="radio"/>	Cystatin C amyloidosis
<input type="radio"/>	Glomerulonephritis
<input checked="" type="radio"/>	AL amyloidosis <b>This is the correct answer</b>

AL amyloidosis is associated with deposition of immunoglobulin light chains and is caused by multiple myeloma.

He has a mixed picture of heart failure and proteinuria which is likely to be due to both cardiac and renal amyloid deposition. Given his degree of hypoalbuminaemia, it is likely that light chains would be easily detectable in the urine.

AA amyloidosis occurs in conjunction with systemic inflammatory conditions, cystatin C amyloidosis in conjunction with Icelandic hereditary cerebral haemorrhage and amyloidosis, and beta protein precursor amyloidosis with Alzheimer's disease and Down's syndrome.

Treatment is driven by chemotherapy for the underlying myeloma.

### Question 127 of 206

You are asked to urgently review a 32-year-old woman who is receiving a blood transfusion following a postpartum haemorrhage which occurred after the birth of her second baby.

Apparently, she required a three unit blood transfusion after the birth of her first child. A short time after the transfusion began she became acutely short of breath, with saturations of only 91% on air, and severe wheezing.

On examination she is pyrexial 37.8°C, her BP is 110/60 mmHg, her pulse 89 and regular. She has marked bilateral wheeze on auscultation of her chest.

Investigations reveal:

<b>Haemoglobin</b>	104 g/L	(11.5-16.0)
<b>White cell count</b>	$8.3 \times 10^9/L$	(4-11)
<b>Platelets</b>	$179 \times 10^9/L$	(150-400)
<b>Serum sodium</b>	138 mmol/L	(135-146)
<b>Serum potassium</b>	3.7 mmol/L	(3.5-5)
<b>Serum creatinine</b>	100 $\mu\text{mol/L}$	(79-118)
<b>CXR</b>	Bilateral pulmonary infiltrates	
<b>PaO<sub>2</sub></b>	8.4 kPa	(10-13)
<b>PaCO<sub>2</sub></b>	5.2 kPa	(4.8-6.1)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute haemolytic transfusion reaction
<input type="radio"/>	Acute non-haemolytic transfusion reaction
<input type="radio"/>	Cardiogenic pulmonary oedema
<input type="radio"/>	IgE mediated transfusion reaction

<input type="radio"/>	Transfusion associated lung injury
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<input checked="" type="radio"/>	Transfusion associated lung injury <b>This is the correct answer</b>
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Transfusion associated lung injury (TRALI) occurs in patients who have received a multi-unit blood transfusion previously and are then re-transfused some time later.

Two hypotheses are proposed for the cause of TRALI, that it is either

- Due to HLA antigens in the donor blood reacting with neutrophil antigens in the patient, leading to neutrophil migration to pulmonary capillaries

or that

- The neutrophils responsible do not actually require donor HLA antigens to react, and are just primed by infection, surgery or inflammation.

What is common to both hypotheses though, is that the neutrophils lead to a local release of cytokines, increased capillary permeability, and non-cardiogenic pulmonary oedema, accounting for the presentation with wheeze and hypoxia which is seen here.

### Question 128 of 206

A 42-year-old man presents with increasing abdominal pain and a feeling of fullness and nausea when he eats. He has also felt constitutionally unwell over the past few weeks and months with some night sweats and gradual weight loss.

On examination his BMI is 21, his BP is 126/82 mmHg, pulse 80 and regular, his temperature is 37.4°C. He has an abdominal fullness with some evidence of ascites.

Investigations show

<b>Haemoglobin</b>	109 g/L	(135-180)
<b>White cell count</b>	$8.9 \times 10^9/\text{L}$	(4-11)

<b>Platelets</b>	188 ×10 <sup>9</sup> /L	(150-400)
<b>ESR</b>	67 mm/hr	(<10)
<b>Serum sodium</b>	137 mmol/L	(135-146)
<b>Serum potassium</b>	4.9 mmol/L	(3.5-5)
<b>Creatinine</b>	115 µmol/L	(79-118)
<b>Alanine aminotransferase</b>	85 U/L	(5-40)
<b>Colonoscopy</b>	Caecal mass, suggestive of Burkitt's lymphoma	

Which translocation is likely to be found in the Burkitt's cells?

(Please select 1 option)

<input checked="" type="radio"/>	2:5
<input type="radio"/>	8:14
<input checked="" type="radio"/>	8:21
<input type="radio"/>	9:21
<input checked="" type="radio"/>	14:11



8:14 This is the correct answer

Burkitt's lymphoma is associated with a t(8;14)(q24;q32) translocation, which is observed in approximately 80% of patients with the disease. What this does is to juxtapose c-Myc, which is a transcription factor responsible for initiating the cell cycle, with the locus for the immunoglobulin heavy chain.

Burkitt's lymphoma, particularly sporadic lymphoma, may be seen in adults and commonly involves the abdominal organs, usually the caecum as seen here, or the distal ileum.

Localised Burkitt's is associated with around a 90% survival rate, although the prognosis is less good in adults.

### Question 129 of 206

A 32-year-old woman presented to the Emergency Department with right upper quadrant pain related to cholecystitis. The pain settled with conservative management, but the surgeons noticed when they admitted her that she appeared to have splenomegaly.

You examine her and confirm that she has an enlarged spleen. On further questioning, she tells you that her father had his spleen removed.

Investigations show:

<b>Haemoglobin</b>	109 g/L	(115-165)
	Spherocytes and reticulocytes seen on film	
<b>Mean corpuscular volume</b>	102 fL	(80-96)
<b>White cell count</b>	$7.9 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$180 \times 10^9/\text{L}$	(150-400)

<b>Serum sodium</b>	141 mmol/L	(135-146)
<b>Serum potassium</b>	4.4 mmol/L	(3.5-5)
<b>Creatinine</b>	90 µmol/L	(79-118)

Which of the following is the most appropriate next investigation?

(Please select 1 option)

<input type="radio"/>	Autoimmune profile
<input type="radio"/>	Bone marrow biopsy
<input type="radio"/>	Coombs' test
<input type="radio"/>	Osmotic fragility test
<input type="radio"/>	Ultrasound scan abdomen
<input checked="" type="radio"/>	Osmotic fragility test <b>This is the correct answer</b>

This patient has a history which is strongly suggestive of hereditary spherocytosis, with increased haemolysis leading to increased risk of gallstones as seen here.

Spherocytosis occurs because of inherited defects in the membrane of red blood cells, leading to reduced cell deformability and this leads to the cells being removed by the spleen, which is the cause of progressive splenic enlargement.

Twenty to 30% of patients have mild disease, and, as in this case, can present later in life, but 60-70% have more severe anaemia and splenic enlargement which leads to presentation in childhood.

Elective splenectomy is often required in severe cases, but patients with mild hereditary spherocytosis (HS) may require no intervention at all.

This question is slightly out of date, but similar ones may still appear in the MRCP. In current clinical practice, most diagnoses can be made based on family history, typical clinical features and laboratory features (spherocytes, increased reticulocytes, raised mean corpuscular haemoglobin concentration). Additional tests are only required for equivocal cases, and these include the cryohaemolysis test and EMA binding or gel electrophoresis of reticulocyte membranes.

The osmotic fragility test is now considered to be unreliable.

### Question 130 of 206

A 72-year-old woman is admitted by the orthopaedic surgeons for a routine left total hip replacement (THR). She has no past medical history of note apart from well-controlled hypertension which is currently managed with a combination of ramipril and amlodipine.

On examination her BP is 142/82 mmHg, her pulse is 75 and regular, her BMI is 23 kg/m<sup>2</sup>. She looks pale, cardiovascular and respiratory examination is unremarkable, but she has splenomegaly on examination of the abdomen.

Investigations show:

<b>Haemoglobin</b>	104 g/L	(115-165)
<b>White cell count</b>	$35.1 \times 10^9/\text{L}$	(4-11)
<b>Lymphocytes</b>	$31.2 \times 10^9/\text{L}$	(1.5-4)
<b>Platelets</b>	$180 \times 10^9/\text{L}$	(150-400)
<b>Serum sodium</b>	138 mmol/L	(135-146)

<b>Serum potassium</b>	4.4 mmol/L	(3.5-5)
<b>Creatinine</b>	115 µmol/L	(79-118)
<b>Bone marrow aspirate</b>	Lymphocytic infiltration	

Which of the following is the most appropriate course of action?

(Please select 1 option)

<input type="radio"/>	Chlorambucil
<input type="radio"/>	Cyclophosphamide
<input type="radio"/>	Lenalidomide
<input type="radio"/>	Proceed with the hip replacement
<input type="radio"/>	Rituximab
<input checked="" type="radio"/>	Proceed with the hip replacement <b>Correct</b>

This patient has chronic lymphocytic leukaemia (CLL).

Indications for intervention are very clear, and the implication, in this case, is that the patient has no symptoms from her CLL.

Guidelines suggest that chemotherapy should be considered when one of the following conditions is satisfied:

- weight loss more than 10%
- extreme fatigue
- progressive marrow failure

- autoimmune anaemia or thrombocytopenia not responding to prednisolone
- progressive splenomegaly
- massive lymphadenopathy or progressive lymphocytosis
- progressive lymphocytosis (an increase of more than 50% in two months or a doubling time of less than six months).

From the history, we are given she currently satisfies none of these conditions and can proceed to THR.

### Question 131 of 206

A 32-year-old woman who has been admitted on two previous occasions with hypertension, agitation and severe abdominal pain is brought to the Emergency Department by her husband.

She has apparently hardly slept over the past few days, staying up all night working and then most recently drinking substantial amounts of alcohol.

On examination, her behaviour strikes you as hypomanic. She has a BP of 155/91 mmHg, and a pulse of 85. Her abdomen is soft, but is diffusely tender with active bowel sounds.

#### Investigations

<b>Haemoglobin</b>	128 g/L	(115-165)
<b>White cells</b>	$11.3 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$204 \times 10^9/\text{L}$	(150-400)
<b>Sodium</b>	131 mmol/L	(135-146)
<b>Potassium</b>	4.4 mmol/L	(3.5-5)
<b>Creatinine</b>	95 $\mu\text{mol/L}$	(79-118)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute intermittent porphyria
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<input type="radio"/>	Hypothyroidism
<input type="radio"/>	Irritable bowel syndrome
<input type="radio"/>	Manic depressive psychosis
<input type="radio"/>	Stimulant abuse
<input checked="" type="radio"/>	Acute intermittent porphyria <b>This is the correct answer</b>

Acute intermittent porphyria (AIP) should be considered in this type of patient, where there are intermittent symptoms characterised by repeated attacks of abdominal pain where no obvious cause is found.

Other features consistent with the diagnosis include:

- agitation
- hypertension
- hyponatraemia, and
- mild leukocytosis.

A range of psychiatric symptoms, including hypomania and delirium may be seen.

Urinary porphobilinogen assay is the optimal way to establish the diagnosis.

Avoidance of precipitants, including alcohol and the oral contraceptive pill, can dramatically reduce the frequency of attacks.

### Question 132 of 206

A 50-year-old man is admitted to the hospital with a third attack of renal stones in the last six months.

He suffers from Crohn's disease and has previously had a limited small bowel resection, but his disease is now quiescent. Apparently, there is a history of high calcium levels in other blood relatives.

On examination, his BP is 115/72 mmHg, his BMI is 19.5, he has a midline scar consistent with a previous laparotomy.

Investigations show:

<b>Haemoglobin</b>	120 g/L	(115-165)
<b>White cell count</b>	$6.4 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$272 \times 10^9/\text{L}$	(150-400)
<b>Serum sodium</b>	138 mmol/L	(135-146)
<b>Serum potassium</b>	4.1 mmol/L	(3.5-5)
<b>Creatinine</b>	85 $\mu\text{mol/L}$	(79-118)
<b>Calcium</b>	2.89 mmol/L	(2.20-2.67)
<b>PTH</b>	Upper limit of normal range	

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Familial hypocalciuric hypercalcaemia
<input type="radio"/>	Primary hyperparathyroidism
<input type="radio"/>	PTHrP levels increased due to underlying malignancy

<input type="radio"/>	Secondary hyperparathyroidism
<input type="radio"/>	Tertiary hyperparathyroidism
<input checked="" type="radio"/>	Familial hypocalciuric hypercalcaemia <b>Correct</b>

Plasma calcium is tightly regulated by parathyroid hormone (PTH) and vitamin D, which act on the gastrointestinal tract, kidney, and bone. PTH releases calcium from bone and inhibits its excretion from the kidney. Vitamin D promotes calcium absorption from the gastrointestinal tract. Plasma calcium levels are detected by a calcium-sensing receptor on the parathyroid glands.

This gentleman has a raised calcium with an inappropriately high PTH. The remainder of his bloods are normal, with no evidence of renal failure or malabsorption.

Familial hypocalciuric hypercalcaemia is an autosomal dominant condition and is the most likely diagnosis in this case.

The disease most often leads to asymptomatic elevated levels of serum calcium, although some patients with the condition may suffer recurrent episodes of renal stones.

The inherited condition is usually caused by a mutation in the calcium-sensing receptor gene. The perceived lack of calcium levels by the parathyroid leads to resetting of calcium and PTH to higher levels. It does not require any treatment.

Primary hyperparathyroidism is caused by parathyroid adenomas or hyperplasia, which results in raised PTH and subsequently raised plasma and urinary calcium. Alkaline phosphatase is raised, and serum phosphate is reduced.

Secondary hyperparathyroidism is compensatory hypertrophy of all four glands due to hypocalcaemia (due to chronic kidney disease, or malabsorption). PTH is raised and calcium is low or normal.

Tertiary hyperparathyroidism develops after a prolonged period of secondary hyperparathyroidism. The parathyroid glands become autonomous and both PTH and calcium are raised.

PTH-related protein is responsible for 80% of hypercalcaemia in malignancy and acts on the same receptors as PTH. It is secreted by squamous cell tumours, breast and renal tumours. Serum calcium is raised, but PTH will be low.

### Question 133 of 206

Choose the correct statement regarding the storage conditions and shelf life of blood products.

(Please select 1 option)

<input type="radio"/>	Fresh frozen plasma is stored below $-30^{\circ}\text{C}$ for up to 24 months
<input type="radio"/>	Fresh frozen plasma is stored below $-25^{\circ}\text{C}$ for up to 36 months
<input type="radio"/>	Platelets are stored at $22^{\circ}\text{C}$ for up to 10 days
<input type="radio"/>	Platelets are stored at $4^{\circ}\text{C}$ for up to 5 days
<input type="radio"/>	Packed red cells are stored at $4^{\circ}\text{C}$ for up to 25 days Incorrect answer selected

<input checked="" type="radio"/>	Fresh frozen plasma is stored below $-25^{\circ}\text{C}$ for up to 36 months This is the correct answer
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Fresh frozen plasma can be stored for up to 36 months below  $-25^{\circ}\text{C}$ . It must not be refrozen once thawed.

The storage period of platelets depends on a number of factors, including the container material, platelet concentration and method of collection. In general, they can be stored at  $22 \pm 2^{\circ}\text{C}$  for up to 5 days with continuous gentle agitation. Storage up to 7 days is possible but increases the risk of bacterial contamination which must be excluded (e.g. using bacterial assays) prior to administration.

Packed red cells may be stored for a maximum of 35 days at  $4 \pm 2^{\circ}\text{C}$  if an adenine supplemented anticoagulant is used; without this the maximum storage period is 28 days.

### Question 134 of 206

Which of the following is true about the manufacture of pooled plasma derivatives?

(Please select 1 option)

<input type="radio"/>	Pooled plasma is often sourced from within the UK
<input type="radio"/>	The end product is a freeze-dried product
<input type="radio"/>	The process does not involve any viral inactivation steps
<input type="radio"/>	These are usually manufactured from 10 donors at a time
<input type="radio"/>	These products have a short half life, typically days

<input checked="" type="radio"/>	The end product is a freeze-dried product <b>This is the correct answer</b>
----------------------------------	---

The plasma derivatives (such as factor VIII) are prepared from several thousand plasma donations, typically 20,000, or 5,000 kg of plasma at a time.

Pooled plasma has been sourced from outside the UK since 1999 to avoid vCJD risks.

The process involves several chemical steps including ethanol extraction, chromatography, and viral inactivation steps which results in a freeze-dried product.

These products have a long shelf life of several months to years.

### Question 135 of 206

Which of the following infusion times would be appropriate during the transfusion of a blood product in a stable patient?

(Please select 1 option)

<input type="radio"/>	A packed cell transfusion should be given over 20 minutes
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<input type="radio"/>	A packed cell transfusion should be given over 90 minutes
<input type="radio"/>	A platelet transfusion should be given over 60 minutes
<input type="radio"/>	A platelet transfusion should be given over 90 minutes
<input type="radio"/>	A platelet transfusion over 120 minutes

<input checked="" type="radio"/>	A packed cell transfusion should be given over 90 minutes <b>This is the correct answer</b>
----------------------------------	---

In a stable patient, red cell packs may be transfused over 90-120 minutes while a platelet transfusion should not take more than 20-30 minutes.

Rapid infusion of red cells or fresh frozen plasma may be required in an acutely bleeding patient but not in this patient who is stable.

### Question 136 of 206

Which of the following is the minimum dataset for identifying a patient and a sample for purpose of a non-emergency blood transfusion?

(Please select 1 option)

<input type="radio"/>	The full name and gender
<input type="radio"/>	The full name, date of birth and patient identity number
<input type="radio"/>	The full name, gender, address and patient identity number
<input type="radio"/>	The full name, gender and patient identity number

<input type="radio"/>	The full name, gender, previous blood grouping details, address and patient identity number
<input checked="" type="radio"/>	The full name, date of birth and patient identity number <b>Correct</b>

Given that the largest number of errors and near misses occur because of mislabelling or mistaken identity of a patient or the sample, a minimum data set is prescribed for transfusion requests.

This involves recording the:

- full name
- date of birth
- patient identity number, and
- address (in some areas, such as Wales).

Previous blood grouping details are not required and missing elements of this minimum dataset are not acceptable in the transfusion service.

### Question 137 of 206

For which of the following patients would a gamma irradiated blood product be recommended?

(Please select 1 option)

<input type="radio"/>	A 16-year-old thalassaemic receiving regular transfusions
<input type="radio"/>	A 19-year-old nulliparous female after a road traffic accident
<input type="radio"/>	A 37-year-old patient with Hodgkins' lymphoma receiving chemotherapy
<input type="radio"/>	A 42-year-old lady receiving adjuvant hormonal therapy for breast cancer post radical mastectomy

<input type="radio"/>	Postoperatively for carcinoma of the colon in a 50-year-old male
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<input checked="" type="radio"/>	A 37-year-old patient with Hodgkins' lymphoma receiving chemotherapy <b>This is the correct answer</b>
----------------------------------	--

The most common indications for irradiated blood products include:

- those at risk of transfusion associated with graft versus host disease such as neonates
- those receiving purine analogues based chemotherapy
- Hodgkin's lymphoma
- immunodeficiency states, and
- post bone marrow transplants

The other scenarios described here do not necessarily represent an immunosuppressed state in the list of conditions eligible for an irradiated blood product.

### Question 138 of 206

The blood to be used for an exchange transfusion in a neonate should fulfil which of the following criteria?

(Please select 1 option)

<input type="radio"/>	Any blood less than 5-days-old
<input type="radio"/>	Any plasma reduced whole blood in CPD (citrate phosphate dextrose/anticoagulant)
<input type="radio"/>	Plasma reduced whole blood in CPD less than five days old and irradiated
<input type="radio"/>	Plasma reduced whole blood in CPD less than 5 days old, irradiated and Rh positive
<input type="radio"/>	Plasma reduced whole blood in CPD which is irradiated

<input type="radio"/>	Plasma reduced whole blood in CPD less than five days old and irradiated <b>This is the correct answer</b>
-----------------------	--

An exchange transfusion requires blood which is plasma reduced whole blood, irradiated and less than five days old.

The Rh group should either be Rh negative or identical to the neonate, to avoid haemolytic transfusion reaction in the neonate.

### Question 139 of 206

A patient on a medical ward received a transfusion 48 hours ago for symptomatic anaemia on a background of chronic renal disease and obstructive airways disease.

He gives a history of previous transfusions in the last year.

The patient has now dropped his Hb by 20 g/L compared to his pre-transfusion level and reports a dark coloured urine. The LDH and bilirubin are elevated.

Which of the following is this most likely to represent?

(Please select 1 option)

<input type="radio"/>	Acute haemolytic transfusion reaction
<input type="radio"/>	Acute hepatitis as an infective complication
<input type="radio"/>	Delayed haemolytic transfusion reaction
<input type="radio"/>	Non-haemolytic febrile transfusion reaction
<input type="radio"/>	Transfusion related graft versus host disease

<input checked="" type="radio"/>	Delayed haemolytic transfusion reaction <b>This is the correct answer</b>
----------------------------------	---

This case is an example of delayed haemolytic transfusion reaction which occurs 24 hours after the transfusion.

This happens in a patient who has been previously immunised by transfusions or pregnancy. The antibodies are not detectable initially but become obvious as a secondary immune response to the antigen exposure during the transfusion occurs.

The following should be carried out:

- A haemoglobin level
- Blood film
- LDH
- Direct antiglobulin test
- Renal profile
- Serum bilirubin
- Haptoglobin
- Urinalysis for haemoglobinuria.

The group and antibody screen should be repeated.

A transfusion-associated graft versus host disease and an acute hepatitis are unlikely given the time frame; both would be expected to occur in a week or two.

This is also not an acute haemolysis which would be expected to occur during the transfusion.

Given the rise in bilirubin and LDH, this is a haemolytic reaction.

### Question 140 of 206

The risk of a viral infection transmitted via a transfusion is widely variable.

In the United Kingdom, the approximate risk of transmission of hepatitis B would be best described as which of the following?

(Please select 1 option)

<input type="radio"/>	1 per 1 million donations
<input type="radio"/>	1 per 10 million donations
<input type="radio"/>	1 per 50 million donations

<input type="radio"/>	20 per 1 million donations
<input type="radio"/>	100 per 1 million donations
<input checked="" type="radio"/>	1 per 1 million donations <b>Correct</b>

The common viral infections considered in the infective risks of a blood transfusion are hepatitis B, hepatitis C, and HIV.

The risks are variable depending on the source of donation and the type of testing employed but generally, in the United Kingdom, the risks for hepatitis B are in the order of 1 per 1.3 million donations while those for HIV and hepatitis C are 1 in 6.5 million and 1 in 28 million donations.

A broad knowledge of the risks may be required while consenting a patient for blood transfusion.

### Question 141 of 206

Approximately 1% of pregnant women develop clinically important red cell antibodies, the most common being rhesus antibodies.

The women negative for D antigen develop antibodies on exposure to D positive blood (such as fetomaternal haemorrhage, abortions and transfusions). This increases the risk of haemolytic disease of the newborn (HDN) in subsequent pregnancies.

From the following, choose the correct statement about rhesus antibodies in pregnancy.

(Please select 1 option)

<input type="radio"/>	D positive women are less likely than D negative women to form antibodies to other red cell antigens (such as Kell and Duffy)
<input type="radio"/>	Following delivery, the degree of fetomaternal haemorrhage should be calculated on a blood sample from a D negative mother

<input type="radio"/>	Maternal antibody titres do not predict haemolytic disease of newborn
<input type="radio"/>	Pregnant women should be checked for antibodies at 28 weeks as fetomaternal haemorrhage occurs only after the second trimester.
<input type="radio"/>	The fetal Rh type is not dependent on the paternal Rh grouping

<input checked="" type="radio"/>	Following delivery, the degree of fetomaternal haemorrhage should be calculated on a blood sample from a D negative mother <b>This is the correct answer</b>
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Following delivery, the degree of fetomaternal haemorrhage (FMH) should be calculated on a blood sample from a D-negative mother to adjust the dose of anti-D in the D negative mother delivering a D-positive child.

D-positive women and D-negative women have the same chances of developing antibodies to other red cell antigens.

All pregnant women should have a blood group and antibody screen in their first trimester or at presentation, whichever is earlier.

The fetal Rh type depends on the paternal and maternal Rh typing.

Maternal antibody titres correlate with the degree of haemolytic disease of the newborn (HDN).

### Question 142 of 206

Which of the following is the blood product with the highest risk of transmission of a bacterial infection related to transfusion?

(Please select 1 option)

<input type="radio"/>	Cryoprecipitate
<input type="radio"/>	Factor VIII concentrates

<input type="radio"/>	Fresh frozen plasma
<input type="radio"/>	Packed red cells
<input type="radio"/>	Platelets

<input checked="" type="radio"/>	Platelets <b>This is the correct answer</b>
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Since platelets are stored at room temperature (22°C), the risk of bacterial contamination is highest in this blood product.

In contrast packed red cells are stored at an average of 4°C while fresh frozen plasma, as well as cryoprecipitate, are stored at -20°C.

Factor VIII concentrates are heat inactivated freeze dried products with a minimal risk of bacterial contamination.

### Question 143 of 206

A 56-year-old man is being reviewed for an elective cholecystectomy in the pre-operative clinic.

He has no comorbidities apart from two attacks of cholecystitis in the last 12 months. He has never received a blood transfusion.

The request for the blood bank should include which of the following?

(Please select 1 option)

<input type="radio"/>	Cross match for 3 units only
<input type="radio"/>	Group and save as well as cross match
<input type="radio"/>	Group and save, direct Combs' test (DAT) and a cross match for 2 units

<input type="radio"/>	Group and save, direct Combs' test (DAT) and a cross match for 3 units
<input type="radio"/>	Group and save only
<input checked="" type="radio"/>	Group and save only <b>This is the correct answer</b>

A 'group and save' is adequate for elective surgeries and is standard practice in most modern blood banks. This will involve blood grouping and its confirmation as well as an antibody screen.

Other options include cross match and a direct Coombs' test (also known as the direct antiglobulin test or DAT) which are often done only if the antibody screen test is positive. These are not routinely done for elective surgery unless the patient has had a recent blood transfusion or a history of previous known red cell antibodies.

#### Question 144 of 206

##### Core Questions

The most common error in transfusion according to the SHOT (serious hazards of transfusion) analysis is which of the following?

(Please select 1 option)

<input type="radio"/>	Cross match error in the blood bank laboratory
<input type="radio"/>	Inability to detect antibodies in the blood bank laboratory
<input type="radio"/>	Incorrect indication for transfusion
<input type="radio"/>	Incorrect storage temperature for blood products
<input type="radio"/>	Wrong identification or mislabelling of patient or sample

<input checked="" type="radio"/>	Wrong identification or mislabelling of patient or sample <b>This is the correct answer</b>
----------------------------------	---

Mislabelling of samples, requests, or wrongly identifying recipients are the commonest transfusion errors.

This was borne out in the SHOT study which analysed transfusion errors and 'near misses' in a UK-wide audit.

Other errors such as cross match error, incorrect storage, and transfusion reaction due to an antibody not detected do occur but are rare.

### Question 145 of 206

A regular donor reports yellow discoloration of his eyes and fevers five days after a blood donation.

What would be the next most appropriate course of action for the blood bank medical officer?

(Please select 1 option)

<input checked="" type="radio"/>	Platelets are safe to be released in this situation
<input type="radio"/>	Recall blood products from this donor and arrange for retesting of this donor
<input type="radio"/>	Release all the blood products from this donor if initial testing is negative
<input type="radio"/>	Selected blood products such as red cell packs may be released as these have a small volume of plasma
<input type="radio"/>	The donor needs to be struck off the donor register

<input type="radio"/>	Recall blood products from this donor and arrange for retesting of this donor <b>This is the correct answer</b>
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Depending on the complications developed by the donor, an assessment must be made on how to manage the donor as well as the blood products from the donation.

In this case, the blood products must be recalled until further testing and clarification of the donor illness.

Release of one or any of the blood products must be prevented.

The donor need not be struck off the register at this stage until further testing results are available.

### Question 146 of 206

A 34-year-old man with normal baseline cardiac and respiratory function starts on the ABVD (Adriamycin, bleomycin, vinblastine and dacarbazine) chemotherapy regimen for his stage IIB Hodgkin's lymphoma.

He tolerated the first three cycles of the chemotherapy well.

After completion of the fourth cycle, he presents with exertional dyspnoea, a dry cough, and basal fine crackles. He is afebrile, a chest x ray and ECG are normal.

Which of the following is the most likely diagnostic possibility?

(Please select 1 option)

<input type="radio"/>	Adriamycin related cardiomyopathy
<input type="radio"/>	Bleomycin related pulmonary fibrosis
<input type="radio"/>	Hyperemesis and reflex cough related to dacarbazine
<input type="radio"/>	<i>Pneumocystis jirovecii</i> pneumonia
<input type="radio"/>	Vinblastine related neurotoxicity

<input checked="" type="radio"/>	Bleomycin related pulmonary fibrosis <b>This is the correct answer</b>
----------------------------------	--

Bleomycin related pulmonary fibrosis is a major toxicity of the widely used ABVD regimen for treatment of lymphoma. A high-resolution CT scan and pulmonary function tests are required to diagnose this condition.

Although Adriamycin can cause cardiotoxicity this is unusual at the doses used in this regimen and one would expect abnormalities on the ECG.

He is afebrile so pneumocytis is less likely, although it needs to be considered in the differential.

There is no history of hyperemesis given and a vinblastine neuropathy is unlikely to present as acute shortness of breath.

#### Question 147 of 206

Core Questions

A mild lymphocytosis of  $15 \times 10^9/l$  with a few smear cells is reported on a full blood count result in a 70-year-old asymptomatic man attending clinic for an annual review.

Which of the following would be the essential investigation to establish a diagnosis of chronic lymphocytic leukaemia (CLL)?

(Please select 1 option)

<input type="radio"/>	CT scan of chest abdomen and pelvis
<input type="radio"/>	Lactic dehydrogenase (LDH) levels
<input type="radio"/>	Peripheral blood flow cytometry
<input type="radio"/>	Presence of palpable cervical lymphadenopathy
<input type="radio"/>	Presence of smear cells on the blood film



Peripheral blood flow cytometry **Correct**

Flow cytometry showing a specific pattern of monoclonal B cell proliferation (CD19/5 coexpressing, CD23 positive, light chain restricted B cell population) is diagnostic of CLL.

CT scan and LDH are investigations needed to complete staging but not essential for diagnosis.

Smear cells are reported in other lymphoproliferative as well as benign lymphocytosis and merely indicate fragile lymphocytes which are artefactually smeared on the glass slide.

Cervical lymphadenopathy may be seen in CLL but can also be seen in any other cause of lymphadenopathy (for example, viral infections, adenopathy secondary to local dental infection).

### Question 148 of 206

A 61-year-old man presents with haematuria. He is on warfarin for chronic atrial fibrillation.

His FBC shows a Hb of 112 g/L and his INR is 9; the patient is haemodynamically stable.

The consultant on take advises that this patient needs reversal of the warfarin.

Which of the following would be the blood product/s of choice?

(Please select 1 option)



Cryoprecipitate



Packed cells



Platelets



Prothrombin concentrate (Octaplex)



Recombinant factor VII

<input checked="" type="radio"/>	Prothrombin concentrate (Octaplex) <b>This is the correct answer</b>
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Prothrombin concentrates are products of choice for warfarin reversal in the setting of active bleeding and a markedly raised INR.

While packed cells are important to treat significant bleeding, it would not be indicated at this stage.

Cryoprecipitate, recombinant factor VII and platelets are not indicated for warfarin reversal.

### Question 149 of 206

#### Core Questions

A 40-year-old gentleman presents to the Emergency Department with a two-week history of lethargy, low-grade fever and gum bleeding. He is obtunded.

His full blood count shows a white cell count of  $350 \times 10^9/L$ , haemoglobin of 54 g/L and a platelet count of  $23 \times 10^9/L$ .

Which of the following would be the most appropriate treatment option in this case?

(Please select 1 option)

<input type="radio"/>	Cytotoxic chemotherapy
<input type="radio"/>	Intravenous broad-spectrum antimicrobials
<input type="radio"/>	Leukapheresis followed by cytotoxic chemotherapy
<input checked="" type="radio"/>	Transfusion of three units of red cell concentrate
<input type="radio"/>	Transfusion of one adult therapeutic dose of single donor platelets

<input checked="" type="radio"/>	Leukapheresis followed by cytotoxic chemotherapy <b>This is the correct answer</b>
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This question covers the presentation of acute leukaemia with hyperleukocytosis.

Acute leukaemia can present with evidence of hyperleukocytosis. There is a predominance of CNS and chest symptomatology, and management should include reduction of the white cell mass by leukapheresis until the appropriate diagnosis is reached, whence the effect of leukapheresis should be consolidated with the appropriate cytotoxic therapy.

Transfusion of red cell concentrate can worsen the hyperviscosity; thus transfusion of three units of red cell concentrate is incorrect.

Whereas transfusion of platelet support and antimicrobials is also indicated, the most appropriate treatment would be leukapheresis followed by cytotoxics in the acute setting, thus eliminating cytotoxic chemotherapy, intravenous broad-spectrum antimicrobials and transfusion of one adult therapeutic dose of single donor platelets.

### Question 150 of 206

A 25-year-old gentleman with Burkitt's lymphoma is admitted and commenced on induction chemotherapy.

Within 48 hours it is noticed that his urine output is dropping to 20 ml/hr.

Further investigation shows:

<b>Potassium</b>	6.5 mmol/L	(3.5-4.9)
<b>Calcium</b>	1.5 mmol/L	(2.2-2.6)
<b>Phosphate</b>	4 mmol/L	(0.8-1.4)
<b>Creatinine</b>	250 µmol/L	(60-110)

Which of the following is the most appropriate management of this complication?

(Please select 1 option)

<input type="radio"/>	Allopurinol and intravenous hydration
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<input type="radio"/>	Intravenous hydration with 3 L/m <sup>2</sup> and rasburicase
<input type="radio"/>	Intravenous hydration with 3 litres per day
<input type="radio"/>	Rasburicase only
<input type="radio"/>	Urinary alkalinisation

<input checked="" type="radio"/>	Intravenous hydration with 3 L/m <sup>2</sup> and rasburicase <b>This is the correct answer</b>
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This question concerns the management of acute tumour lysis syndrome (ATLS).

Acute tumour lysis syndrome is a common complication of haematological tumours which have a high proliferation index, for example, Burkitt's lymphoma, hyperleukocytic acute myelogenous leukaemia (AML), diffuse large B-cell lymphoma.

Management revolves around institution of aggressive hydration, aiming for 3 L/m<sup>2</sup> control of electrolyte disturbances (typically, hypocalcaemia, hyperphosphataemia, hyperkalaemia and uraemia) and clearance of the increased metabolic load with rasburicase, a specific recombinant enzyme.

The incorrect answer options omit important aspects of the holistic management of acute tumour lysis syndrome.

### Question 151 of 206

#### Core Questions

A 55-year-old gentleman presents to his GP with a six-month history of lethargy and left upper quadrant abdominal discomfort.

A blood count shows the following:

<b>White cell count</b>	350 ×10 <sup>9</sup> /L	(4-11)
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<b>Haemoglobin</b>	105 g/L	(130-180)
<b>Platelet count</b>	$223 \times 10^9/\text{L}$	(150-400)

A bone marrow aspirate shows increased granulocytic precursors and less than 5% blasts. Molecular studies show the patient to be BCR-ABL transcript positive.

Which of the following is the most appropriate therapy?

(Please select 1 option)

<input type="radio"/>	Chemotherapy
<input type="radio"/>	Haemopoietic stem cell transplant
<input type="radio"/>	Hydroxycarbamide
<input type="radio"/>	Interferon
<input type="radio"/>	Treatment with tyrosine kinase inhibitor, e.g.imatinib
<input checked="" type="radio"/>	Treatment with tyrosine kinase inhibitor, e.g.imatinib <b>This is the correct answer</b>

The above presentation and laboratory findings are typical for chronic phase chronic myelogenous leukaemia (CML).

Chemotherapy is incorrect because chemotherapy is only used in the blast crisis phase of CML.

Hydroxycarbamide and interferon are now outdated treatments for CML.

Stem cell transplant is not performed first in patients with CML since the advent of specifically targeted therapy for the BCR-ABL transcript positive leukaemias, that is, tyrosine kinase inhibitors, which are now the gold standard therapy for CML.

Hence treatment with tyrosine kinase inhibitor is the correct answer.

### Question 152 of 206

#### Core Questions

A 75-year-old lady is brought to the Emergency Department by her next of kin after a three-week history of having "gone off her feet".

A history of back pain radiating anteriorly around her chest and bilateral weakness of her legs is elicited. Physical examination shows a paraparesis.

Blood investigations are notable for haemoglobin of 95 g/L, serum calcium of 3.6 mmol/L and a creatinine of 250 µmol/L.

Which of the following would be the most appropriate initial investigation?

(Please select 1 option)

<input type="radio"/>	Bone marrow biopsy
<input type="radio"/>	Serum protein electrophoresis, quantitative immunoglobulins and serum free light chains
<input type="radio"/>	CT chest, abdomen, pelvis
<input type="radio"/>	Urgent magnetic resonance imaging of her spine
<input type="radio"/>	Urine for creatinine clearance and Bence Jones protein

<input checked="" type="radio"/>	Urgent magnetic resonance imaging of her spine <b>This is the correct answer</b>
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The combination of hypercalcaemia, anaemia and renal failure in a patient presenting with spinal cord compression should lead you to consider a diagnosis of multiple myeloma.

Multiple myeloma is a plasma cell disorder with a malignant clone producing a monoclonal paraprotein. Clinical manifestations relate both to substances secreted by the plasma cells and effects of marrow infiltration. Complications include pathological fractures, hyperviscosity syndrome, hypercalcaemia, renal impairment, bone pain, and recurrent infections. Spinal cord compression can develop due to vertebral compression fractures or vertebral plasmacytomas.

An urgent MRI of the spine is indicated to determine whether spinal cord compression is present in view of this para neurology. Bone marrow biopsy, serum protein electrophoresis, quantitative immunoglobulins and serum free light chains and urine for creatinine clearance and Bence Jones protein should all be done following this to determine if myeloma is the underlying diagnosis, and to help guide further treatment. CT can be used to delineate the extent of disease but is not a first line investigation for myeloma or spinal cord compression.

It is also important to realise that this level of hypercalcaemia is potentially life-threatening, with risk of arrhythmia or coma. Immediate treatment is with intravenous hydration (rapidly) followed by intravenous bisphosphonate.

### Question 153 of 206

A 62-year-old gentleman is being investigated for normochromic, normocytic anaemia. He is diagnosed with diabetes mellitus type II and essential hypertension.

His haemoglobin is stable at 95 g/L (normal range 130-162 g/L), his creatinine clearance is calculated at 45 ml/min (normal range 97-137 ml/min), ferritin at 50 µg/L (normal range 12-300 µg/L) and his serum erythropoietin level comes back at 8 (normal range: 4-24 mU/mL).

Which of the following is the most appropriate management?

(Please select 1 option)

<input type="radio"/>	Check haemoglobin at 6-monthly intervals
<input type="radio"/>	Commencement of subcutaneous darbepoietin
<input type="radio"/>	Intravenous iron supplementation
<input type="radio"/>	Transfusion aiming for Hb of 100-120 g/L

<input type="radio"/>	Transfusion aiming for Hb of 120-140 g/L
<input checked="" type="radio"/>	Intravenous iron supplementation <b>This is the correct answer</b>

This patient has CKD stage 3A (borderline 3B). Renal-related anaemia can start to develop at this stage as alteration in erythropoietin production occurs. It is worsened by reduced dietary intake of iron due to anorexia, impaired intestinal absorption of iron, toxic effect of uraemia on erythroid precursors and reduced red blood cell survival.

It is imperative that renal patients avoid repeated blood transfusion, unless in extremis, so that future renal transplantation will not be precluded by allo-sensitisation.

Before initiation of recombinant erythropoiesis-stimulating agents the patient should be iron replete. The serum ferritin and transferrin saturation should be checked, as most patients will be iron deficient.

Targets for treatment are:

- Haemoglobin 105-125 g/L
- Ferritin: >100 µg/L in pre-dialysis and peritoneal dialysis patients, >200 µg/L in haemodialysis patients
- Transferrin saturation >20%

This patient should also be referred to a nephrologist, as early assessment of the causes of his renal impairment is beneficial. Patients with CKD stage 3A, who are non-proteinuric, have a low risk of progression and can usually be managed in the community following an initial assessment by a nephrologist.

Those with proteinuria are usually managed in secondary care, as the protein is directly toxic to the tubules and this typically results in progression of renal impairment.

### Question 154 of 206

A 6-month-old baby is noticed to be pale and listless.

His complete blood count shows haemoglobin of 60 g/L, and his blood picture shows a hypochromic, microcytic picture. Genetic testing shows the  $\beta^0\beta^0$  genotype.

Which statement is correct with regards to this haematological disorder?

(Please select 1 option)

<input type="radio"/>	A transfusion programme with iron chelation is the best initial approach
<input type="radio"/>	Iron chelation is only possible with subcutaneous or intravenous infusion of desferrioxamine
<input type="radio"/>	The parents and other siblings should not be screened by genetic testing
<input type="radio"/>	There is no increased risk of gallstone formation or bone deformities
<input type="radio"/>	Transfusion support should be used sparingly considering the risks of transmission of infections and iron overload

<input checked="" type="radio"/>	A transfusion programme with iron chelation is the best initial approach <b>This is the correct answer</b>
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This question relates to the management of severe beta thalassaemia major.

Beta thalassaemia major is characterised by anaemia, splenomegaly, bone deformities and early death if not treated appropriately.

Treatment revolves around lifesaving red cell concentrate support, with the inherent development of transfusional iron overload, which can be managed with iron chelation, both intravenous/subcutaneous (desferrioxamine) or oral (deferasirox).

The next of kin should be offered screening.

Regular transfusion with attention to iron chelation is the mainstay of treatment, although haemopoietic stem cell transplantation has a possible role with curative intent, hence a transfusion programme with iron chelation is the best initial approach.

### Question 155 of 206

Core Questions

A 10-year-old boy is noticed to be jaundiced on return from a holiday in Africa with his parents. He is on antimalarial prophylaxis.

His complete blood count shows haemoglobin of 80 g/L, with Heinz bodies and blister cells on blood film examination.

Which of the following relates to this disorder?

(Please select 1 option)

<input type="radio"/>	It is most commonly precipitated by peas
<input type="radio"/>	The antimalarial prophylaxis has no relation to the laboratory findings
<input type="radio"/>	This is a common autosomal dominant disorder
<input type="radio"/>	Transfusion is strictly merited in each case
<input type="radio"/>	Treatment involves strict avoidance of known precipitants

<input checked="" type="radio"/>	Treatment involves strict avoidance of known precipitants <b>This is the correct answer</b>
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This question relates to the management of G-6-PD deficiency.

G-6-PD is the most common inherited enzyme defect in humans; an X-linked inheritance pattern.

It is mostly commonly precipitated by several classes of drugs, including antimalarials and is also associated with ingestion of broad beans (favism).

Treatment revolves around avoidance of all known precipitating factors, and blood product support should only be given in unstable, symptomatic patients.

**Question 156 of 206**  
Core Questions

Which of the following observations best describes the relationship between malaria and HbS?

(Please select 1 option)

<input type="radio"/>	HbS protects against all complications of falciparum malaria
<input type="radio"/>	Malaria causes damage to red cell DNA, which is why sickle cell disease is more common in malarial regions
<input type="radio"/>	Only HbSS protects against malaria, HbAS is not protective
<input type="radio"/>	Patients with sickle cell disease do not get malaria
<input type="radio"/>	Sickle cell disease is most common in regions where <i>P.falciparum</i> malaria is endemic and in ethnic groups that have migrated from these areas

<input checked="" type="radio"/>	Sickle cell disease is most common in regions where <i>P.falciparum</i> malaria is endemic and in ethnic groups that have migrated from these areas <b>This is the correct answer</b>
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The sickle cell gene is most prevalent in areas where malaria is also prevalent. This genetic abnormality is not caused by malaria, but the selective advantage of the carrier state in malarial regions has allowed it to persist in the gene pool (positive selective evolutionary pressure).

Patients with sickle cell trait have just as much risk of contracting *P. falciparum* malaria compared with patients with HbAS or HbAA.

However, the reduced red cell life cycle in HbAS reduces parasitaemia, which reduces the risk of severe disease and neurological complications (for example, seizures and coma).

Patients with HbSS are at higher risk of severe malaria with complications and have a higher mortality rate.

**Question 157 of 206**

Which of the following is a feature of haemoglobin S?

(Please select 1 option)

<input type="radio"/>	Has a higher affinity for oxygen than HbA
<input type="radio"/>	It is more negatively charged than HbA and as a result, less soluble
<input type="radio"/>	Is a result of a point mutation
<input type="radio"/>	It has the effect of shifting the oxygen dissociation curve to the left
<input type="radio"/>	It contains two $\alpha$ -like globins and two $\beta$ -like globins and two haem molecules

<input checked="" type="radio"/>	Is a result of a point mutation <b>This is the correct answer</b>
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HbS has the following properties:

- it is less negatively charged, due to the loss of glutamate for valine
- it polymerises with adjacent HbS
- the loss of the negative charge and the configuration of HbS makes it less soluble than HbA
- it has lower affinity for oxygen (right-shift of the oxygen-dissociation curve), which increases the risk of desaturation, but improves the yield of oxygen to the tissues
- it is the result of a point mutation substituting glutamate for valine at position 6, and
- it contains two  $\alpha$ -like globins and two  $\beta$ -like globins and four haem molecules.

### Question 158 of 206

A couple who are expecting their first child present to you for advice.

Both parents are known to be carriers of sickle cell trait HbS and want to know if their child will inherit the disease.

Which of the following do you advise?

(Please select 1 option)

<input type="radio"/>	There is no chance their child will inherit the
<input type="radio"/>	There is a 25% chance their child will inherit the disease
<input type="radio"/>	There is a 50% chance their child will inherit the disease
<input type="radio"/>	There is a 75% chance their child will inherit the disease
<input type="radio"/>	There is a 100% chance their child will inherit the disease

<input checked="" type="radio"/>	There is a 25% chance their child will inherit the disease <b>This is the correct answer</b>
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This question is slightly ambiguous in the way it is worded but is, unfortunately, typical of those found in the MRCP exam.

If both parents carry the sickle cell gene there is a 25% chance that their child will inherit sickle cell disease since the gene is inherited in an autosomal recessive fashion.

There is a 25% chance the baby will not inherit any affected genes and a 50% chance they will have sickle cell trait.

Although there is no primary prevention for sickle cell disease genetic counselling can help advise heterozygous parents.

Prenatal diagnosis is available by chorionic villus sampling at 8-10 weeks gestation or by amniocentesis at 14-16 weeks gestation.

### Question 159 of 206

A pregnant woman attends for her booking antenatal appointment. She lives and is being treated within a high prevalence trust.

How will screening for sickle cell disease be undertaken?

(Please select 1 option)

<input type="radio"/>	Amniocentesis cannot distinguish whether the fetus has sickle cell trait or sickle cell disease
<input type="radio"/>	It will depend on the family origin of herself and her partner
<input type="radio"/>	She will automatically be offered chorionic villus sampling at 8-10 weeks gestation
<input type="radio"/>	She will first be screened for sickle cell carrier status. If that test is positive, her partner will be screened, and only if both are positive will she be offered chorionic villus sampling or amniocentesis
<input type="radio"/>	The screening only detects HbS. It does not detect any other haemoglobinopathies

<input checked="" type="radio"/>	She will first be screened for sickle cell carrier status. If that test is positive, her partner will be screened, and only if both are positive will she be offered chorionic villus sampling or amniocentesis <b>This is the correct answer</b>
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In low prevalence trusts, laboratory screening is only carried out if the baby is identified as being at risk of a haemoglobinopathy based on the family origin questionnaire, and a routine full blood count from the mother.

In high prevalence trusts, all women undergo the initial laboratory screening to identify if the mother carries the sickle cell gene, regardless of family origin. However, the family origin questionnaire still needs to be completed to facilitate diagnosis of the type of haemoglobinopathy.

The father is tested for carrier status only if the mother is found to be a carrier. If both are found to be carriers this is confirmed by genetic testing before offering chorionic villus sampling (CVS) (8-10 weeks) or amniocentesis (14-16 weeks).

**Question 160 of 206**

The mother of a 16-year-old boy with sickle cell disease comes to your practice and asks for advice with regard to the vaccination requirements of her son.

He has had all of his childhood immunisations on schedule.

Which of the following advice do you give?

(Please select 1 option)

<input type="radio"/>	Usual childhood immunisation schedule is all that is required
<input type="radio"/>	Usual childhood immunisations and meningococcal C vaccine
<input type="radio"/>	Usual childhood immunisations and yearly influenza vaccine
<input type="radio"/>	Usual childhood immunisations, yearly influenza vaccine, five yearly Pneumovax vaccine
<input type="radio"/>	Usual childhood immunisations, five yearly Pneumovax vaccine and meningococcal C vaccine

<input checked="" type="radio"/>	Usual childhood immunisations, yearly influenza vaccine, five yearly Pneumovax vaccine <b>This is the correct answer</b>
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Vaccinations should usually be administered at general practice.

All adults who are hyposplenic, including patients with sickle cell disease, need:

- yearly influenza vaccine
- pneumococcal C vaccine, (adults and children over 2 years) repeated every five years
- *haemophilus influenzae* type b; if not already given as part of childhood immunisation
- conjugated meningococcal C vaccine; if not already given as part of childhood immunisation, and
- meningococcal ACWY vaccine; if travelling to areas with high risk of meningitis.

Patients with sickle cell disease are hyposplenic, and have additional lifelong requirements.

All hyposplenic patients should be offered meningococcal ACWY vaccine if travelling to areas at high risk of meningitis.

Meningococcal C vaccine is a part of primary immunisation schedule which this young boy should have had already. Had this young boy not been up to date with his childhood immunisation schedule, then he should have a single dose.

Although patients with sickle cell disease do need the yearly influenza vaccination, they also need five yearly Pneumovax.

This young boy is up to date with his immunisation and therefore should not need additional meningococcal C vaccination.

### Question 161 of 206

Which of the following are features of acute chest syndrome?

(Please select 1 option)

<input type="radio"/>	Chest pain
<input type="radio"/>	Evidence of new infiltration on CXR
<input type="radio"/>	Fever
<input type="radio"/>	Shortness of breath
<input type="radio"/>	All of the above

<input checked="" type="radio"/>	All of the above <b>This is the correct answer</b>
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Acute chest syndrome, a complication of sickle cell disease, is defined as a 'new infiltrate consistent with consolidation at least segmental in size, and one of chest pain, a temperature  $> 38.5^{\circ}\text{C}$ , tachypnoeic, wheezing or cough'.

It is important to remember that not all of the above features will be present at the same time, CXR changes often lag behind. The key is to have a high index of suspicion and monitor vital signs particularly oxygen saturations regularly and anticipate development of possible acute chest syndrome. Early recognition and treatment is life-saving.

Chest pain is often a feature of acute chest syndrome, either from the onset or presenting later during the course of disease.

Shortness of breath is an important feature of acute chest syndrome and one of the main markers of deterioration indicating the need for possible exchange transfusion. All sickle patients should have their oxygen saturations measured regularly on air.

Fever, usually a temperature of greater than 38.5°C, is another recognised feature of acute chest syndrome. All patients with temperatures more than 38°C should have cultures sent.

Although new infiltrates are a characteristic feature of acute chest syndromes, it is important to remember that they can lag behind, and treatment should not be delayed in the absence of CXR changes if all other clinical signs suggest acute chest syndrome.

Acute chest syndrome is a combination of signs and symptoms, not all of them need to be present for a diagnosis to be made.

### Question 162 of 206

#### Core Questions

Which of the following investigations is not carried out routinely for a patient with an acute sickle cell crisis?

(Please select 1 option)

<input type="radio"/>	Bone x ray
<input type="radio"/>	Cross match
<input type="radio"/>	Cultures
<input type="radio"/>	Full blood count
<input type="radio"/>	Reticulocyte count

<input checked="" type="radio"/>	Bone x ray <b>Correct</b>
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Although bone x rays can show bone infection and avascular necrosis they are not done routinely as they will not aid management in the majority of patients presenting with a sickle cell crisis.

Full blood count is vital to establish any acute worsening of the patient's anaemia. White cell count may be raised in infection.

Reticulocyte count is raised in haemolysis and splenic sequestration and decreased in aplastic crises.

Cultures are essential in patients in whom infection is suspected. Cultures will confirm the pathogens present and give sensitivities.

Cross matching the patient is important as they may require a blood transfusion.

### Question 163 of 206

A 16-year-old girl of African origin presents to the Emergency Department with a one-week history fever and lethargy.

Shortly before developing her symptoms she received a course of antibiotics from her GP for an upper respiratory infection. She also complains of two to three days of pain and swelling in her hands. The patient tells you that she has had similar attacks before.

On examination she is pyrexial, with a heart rate of 109 and oxygen saturations of 91% on air. There is painful dactylitis of both her hands. The remainder of her examination was normal.

Initial investigations reveal:

<b>Haemoglobin</b>	93 g/L	(115-165)
<b>Reticulocytes</b>	8%	(0.5-2.4)
<b>White cell count</b>	$13 \times 10^9/L$	(4-11)

ECG, urinalysis and electrolytes are normal. C-reactive protein is 76.

You decide to treat the patient as a sickle cell crisis.

Which treatment would you start in the Emergency Department?

(Please select 1 option)

<input type="radio"/>	Analgesia
<input type="radio"/>	Analgesia and oxygen
<input type="radio"/>	Analgesia, oxygen and hydration
<input type="radio"/>	Analgesia, oxygen, hydration, and antibiotics
<input type="radio"/>	Analgesia, oxygen, hydration, antibiotics, and hydroxycarbamide
<input checked="" type="radio"/>	Analgesia, oxygen, hydration, and antibiotics <b>This is the correct answer</b>

The correct management of a sickle cell crisis would entail oxygenation, hydration with careful management of fluid balance, analgesia, predominantly based on opioids, and blood product support, including if required exchange transfusion to get the HbS fraction to less than 30%.

HbF switching therapies such as hydroxycarbamide are not instituted acutely.

**Analgesia:** start with paracetamol and then add in a non-steroidal anti-inflammatory, for example, ibuprofen. If this does not control the pain then opioid analgesics should be used, for example, morphine sulphate. Often patients can give you information regarding which analgesics work for them.

**Oxygen:** the patient is hypoxic and will benefit from oxygen therapy. A rate of 2 L/min given via a nasal cannula should be started.

**Hydration:** This is important to correct any intravascular depletion. Oral fluid therapy may be sufficient but if the patient is severely dehydrated or intravenous therapy is required because they are unable to take oral fluids.

**Antibiotics:** Antibiotics should be started if there is evidence of infection, for example, green sputum, positive urinalysis, pyrexia, or raised inflammatory markers. Start with broad spectrum antibiotics and rationalise once sensitivities become available.

Hydroxycarbamide (and bone marrow transplantation) have roles to play in the management of sickle cell disease but they are not used in the acute setting.

Blood transfusion in this patient should be considered as she is anaemic with a raised reticulocyte count but you must also take into account the clinical condition of the patient.

### Question 164 of 206

What is the mechanism of action of hydroxycarbamide in the setting of its use in sickle cell disease?

(Please select 1 option)

<input type="radio"/>	Causing vasodilation
<input type="radio"/>	Decreasing the tendency of HbS to polymerise
<input type="radio"/>	Increasing the life span of sickle shaped redblood cells
<input type="radio"/>	Reducing the permeability of red blood cellmembranes
<input type="radio"/>	Stimulation of the production of fetal haemoglobin
<input checked="" type="radio"/>	Stimulation of the production of fetal haemoglobin <b>This is the correct answer</b>

Stimulation of the production of fetal haemoglobin is its use in sickle cell anaemia; its usual mode of action is on its reduction of production of deoxyribonucleotides via inhibition of the enzyme ribonucleotide reductase. Hydroxycarbamide works by stimulating the production of fetal haemoglobin which protects against sickling.

In HbS the negative charge is lost and this removes the inhibition to polymerise.

HbS polymers interact with the red blood cell membrane creating temporary pores thus increasing permeability.

HbS has a life span of 30 days compared to the normal 120 days.

Vasodilation is caused by nitric oxide (endothelial derived relaxing factor).

### Question 165 of 206

A patient on your ward is prescribed warfarin as she has recently been diagnosed with atrial fibrillation. Her desired INR is 2.5.

On the morning ward round, you take the patient's INR which comes back as 5.2 from the laboratory. There are no signs of bleeding.

Which would be your next course of action?

(Please select 1 option)

<input type="radio"/>	Decrease the dose of warfarin
<input type="radio"/>	Do nothing, as there are no signs of bleeding
<input type="radio"/>	Increase the dose of warfarin
<input type="radio"/>	Omit the warfarin
<input type="radio"/>	Start a heparin infusion

<input checked="" type="radio"/>	Omit the warfarin <b>This is the correct answer</b>
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The main adverse effect of all oral anticoagulants is haemorrhage.

Checking the INR and omitting doses when appropriate is essential; if the anticoagulant is stopped but not reversed, the INR should be measured two to three days later to ensure that it is falling.

The following recommendations are based on the result of the INR and whether there is major or minor bleeding; the recommendations apply to patients taking warfarin:

- Major bleeding - omit warfarin; give phytomenadione (vitamin K1) 5-10 mg by slow intravenous injection; give dried prothrombin complex (factors II, VII, IX, and X) 30-

50 units/kg (if dried prothrombin complex unavailable, fresh frozen plasma 15 mL/kg can be given but is less effective).

- INR 8.0, no bleeding or minor bleeding - omit warfarin and give phytomenadione (vitamin K1) 2.5-5 mg by mouth using the intravenous preparation orally [unlicensed use], or 0.5-1 mg by slow intravenous injection (if complete reversal required 5-10 mg by slow intravenous injection); repeat dose of phytomenadione if INR still too high after 24 hours; restart warfarin when INR less than 5.0.
- INR 5.0-8.0, no bleeding - omit warfarin; minor bleeding - omit warfarin and give phytomenadione (vitamin K1) 1-2.5 mg by mouth using the intravenous preparation orally [unlicensed use]; restart warfarin when INR less than 5.0.
- Unexpected bleeding at therapeutic levels - always investigate possibility of underlying cause, for example, unsuspected renal or gastrointestinal tract pathology.

### Question 166 of 206

During the evaluation of a patient who developed hyperkalaemia, you went through the drug chart.

Which of the following items can be continued without the worry of worsening hyperkalaemia?

(Please select 1 option)

<input type="radio"/>	Cyclosporine
<input type="radio"/>	Digoxin
<input type="radio"/>	Ibuprofen
<input type="radio"/>	Spirolactone
<input type="radio"/>	Thyroxine

<input checked="" type="radio"/>	Thyroxine This is the correct answer
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Thyroxine does not cause nor exacerbate hyperkalaemia.

Translocation of potassium from the cells into the extracellular space can occur from digoxin overdose due to its dose-dependent Na-K-ATPase pump inhibition.

Other common mechanisms include impaired urinary potassium excretion, notably hypoaldosteronism.

### Question 167 of 206

A 54-year-old man was electively admitted for hernia repair.

Prior to surgery, you detected a serum phosphate level of 0.76 mmol/L (reference range 0.80-1.5 mmol/L). The remainder of his laboratory tests were normal.

Which would be the most likely cause?

(Please select 1 option)

<input type="radio"/>	Hyperventilation during painful venepuncture by a new F1
<input type="radio"/>	Laboratory error
<input type="radio"/>	Oncogenic hypophosphataemic osteomalacia
<input type="radio"/>	Tumour lysis syndrome
<input type="radio"/>	X linked hypophosphataemic rickets

<input checked="" type="radio"/>	Hyperventilation during painful venepuncture by a new F1 <b>This is the correct answer</b>
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The three major mechanisms of hypophosphataemia are:

- redistribution of extracellular phosphate into cells
- decreased intestinal absorption, and
- depletion due to increased urinary loss.

When a patient hyperventilates, there is a rise in intracellular pH (fall in partial pressure of carbon dioxide, which can readily diffuse across cell membranes). The rise in pH then stimulates phosphofructokinase activity, which in turn activates glycolysis.

Oncogenic hypophosphataemic osteomalacia and x linked hypophosphataemic rickets belong to the third mechanism of urinary excretion, but there are no hints to suggest so in the question.

Tumour lysis syndrome is incorrect because it causes hyperphosphataemia (and hyperkalaemia) instead of low phosphate level.

Laboratory error is possible, but as all other values are normal, this is less likely. The sample should be repeated to confirm the suspicion that this is due to hyperventilation.

### Question 168 of 206

A 62-year-old Caribbean man with new onset type 2 diabetes presents to the Emergency Department.

He has increasing lethargy and tiredness since starting a sulphonylurea a few days earlier.

On examination he has jaundiced sclerae, his BP is 135/72 mmHg, and pulse is 95. His mucous membranes look a little pale.

Investigations show:

<b>Haemoglobin</b>	102 g/L	(13.5-17.7)
	Heinz bodies seen	-
<b>White cell count</b>	$10.2 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$198 \times 10^9/\text{L}$	(150-400)
<b>Sodium</b>	138 mmol/L	(135-146)
<b>Potassium</b>	4.4 mmol/L	(3.5-5)

<b>Creatinine</b>	88 $\mu\text{mol/L}$	(79-118)
<b>Bilirubin</b>	80 $\mu\text{mol/L}$	(<17)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Autoimmune haemolytic anaemia
<input type="radio"/>	Cold agglutinin disease
<input type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency
<input type="radio"/>	Obstructive jaundice
<input type="radio"/>	Paroxysmal nocturnal haemoglobinuria
<input checked="" type="radio"/>	Glucose-6-phosphate dehydrogenase deficiency <b>This is the correct answer</b>

G-6-PD deficiency is more common in patients of Afro-Caribbean origin. Sulphonylureas are a class of drugs associated with increased risk of red cell oxidation and the absence of G-6-PD leads to haemolytic anaemia and increased levels of unconjugated bilirubin.

Autoimmune haemolytic anaemia would be associated with a more chronic course, and the close proximity to use of sulphonylurea is much more suggestive of G-6-PD deficiency.

Cold agglutinins are associated with mycoplasma or haematological malignancy.

Obstructive jaundice would not usually be associated with anaemia.

Paroxysmal nocturnal haemoglobinuria (PNH) presents with episodes of haemolysis.

Venous thrombosis usually presents at a younger age.

### Question 169 of 206

A 45-year-old man is to undergo knee surgery. He has a history of factor IX deficiency. You are concerned about the prospect of significant bleeding during surgery.

Which of the following is most likely to reduce his risk of bleeding?

(Please select 1 option)

<input type="radio"/>	Mefenamic acid
<input type="radio"/>	Tranexamic acid
<input type="radio"/>	Vasopressin
<input type="radio"/>	Vitamin K
<input type="radio"/>	von Willebrand factor

<input checked="" type="radio"/>	Tranexamic acid <b>This is the correct answer</b>
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Tranexamic acid competitively inhibits activation of plasminogen, thereby reducing the conversion of plasminogen to plasmin. This results in slower degradation of fibrin clots, fibrinogen and other plasma proteins including factors V and VIII. As such it may be of value in patients undergoing surgery who have inherited factor IX deficiency in order to reduce the perioperative risk of bleeding.

Recombinant factor IX is of course also an option where it is available, although patients have a high tendency to form neutralising antibodies to factor IX.

Vasopressin is associated with a significant increase in levels of both factor VIII and von Willebrand factor in haemophilia A.

Any increase seen in factor IX levels after vasopressin is however much more minor. As such tranexamic acid is a much more useful therapeutic choice.

None of the other options given has any role in the management of factor IX deficiency.

### Question 170 of 206

You are evaluating a new agent which is thought to improve the recognition of foreign antigen by antigen presenting cells (APCs).

Which of the following correctly represents one aspect of the physiology of APCs?

(Please select 1 option)

<input type="radio"/>	Antigen is presented via MHC class I complexes
<input type="radio"/>	Antigen presented on APCs is recognised by CD4 positive cells
<input type="radio"/>	APCs are required before a response to viruses can be generated
<input type="radio"/>	Direct antigenic stimulation still requires APCs
<input type="radio"/>	Follicular dendritic cells express MHC class 2

<input checked="" type="radio"/>	Antigen presented on APCs is recognised by CD4 positive cells <b>This is the correct answer</b>
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Extracellular antigen which is not directly recognised as foreign requires processing by APCs to generate an immune response. This process involves these cells expressing antigenic peptides in conjunction with MHC class II.

Antigen is presented via MHC class II complexes, MHC class I aids in the recognition of virally infected cells.

Direct stimulation of an immune response may occur in the absence of APCs.

Follicular dendritic cells are a distinct lineage which do not express MHC class II, but can still bind the Fc portion of antibodies.

APCs are not required before an immune response to viral infection can be successfully mounted.

### Question 171 of 206

A 31-year-old woman comes to the clinic for review of chronic diarrhoea. She tells you she is opening her bowels some four to five times per day and has lost 5 kg in weight over the past six months.

There is no blood and the diarrhoea has a strong smell and is difficult to flush away.

On examination her BP is 110/70 mmHg, pulse is 75 and regular, her BMI is 21.

Investigations show:

<b>Haemoglobin</b>	108 g/L	(115-160)
<b>MCV</b>	75 fL	(80-96)
<b>White cell count</b>	$9.3 \times 10^9/\text{L}$	(4-11)
<b>ESR</b>	41 mm/hr	(<10)
<b>Platelets</b>	$182 \times 10^9/\text{L}$	(150-400)
<b>Sodium</b>	139 mmol/L	(135-146)
<b>Potassium</b>	3.6 mmol/L	(3.5-5)
<b>Creatinine</b>	115 $\mu\text{mol/L}$	(79-118)
<b>Albumin</b>	24 g/L	(35-50)

Which of the following investigations is likely to be most useful in confirming the diagnosis?

(Please select 1 option)

<input type="radio"/>	Anti-endomysial antibodies
<input type="radio"/>	Colonoscopy
<input type="radio"/>	CT abdomen
<input type="radio"/>	Faecal elastase
<input type="radio"/>	Faecal fat estimation

<input checked="" type="radio"/>	Anti-endomysial antibodies <b>This is the correct answer</b>
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The age of the patient and symptoms consistent with malabsorption, coupled with low albumin and iron deficiency anaemia fit best with a diagnosis of coeliac disease. As such anti-endomysial antibodies are the most appropriate of the investigations listed to confirm the diagnosis.

Colonoscopy is useful only if lower GI pathology is suspected, and CT abdomen is not very useful to confirm a diagnosis of coeliac.

Faecal elastase is a test for pancreatic insufficiency, and whilst faecal fat estimation will be useful in confirming malabsorption, it will not differentiate between pancreatic pathology and small bowel disease.

### Question 172 of 206

A 19-year-old woman presents for the third time in the past eight months with acute abdominal pain and severe agitation. On the two previous occasions, she was admitted by the surgeons and discharged without significant intervention.

She has started the oral contraceptive pill within the last year. According to her mother, the local GP has considered medicating her because of increasing anxiety.

On examination her BP is 155/82 mmHg, pulse is 90 and regular, BMI 22. Her abdomen is generally tender although there are active bowel sounds.

Investigations show:

<b>Haemoglobin</b>	120 g/L	(115-160)
<b>White cell count</b>	$9.3 \times 10^9/\text{L}$	(4-11)
<b>Platelets</b>	$182 \times 10^9/\text{L}$	(150-400)
<b>Sodium</b>	135 mmol/L	(135-146)
<b>Potassium</b>	3.9 mmol/L	(3.5-5)
<b>Creatinine</b>	92 $\mu\text{mol/L}$	(79-118)

You give her opiates for pain.

Which of the following is the most important additional therapy during this acute attack?

(Please select 1 option)

<input type="radio"/>	IV cefuroxime and metronidazole
<input type="radio"/>	IV glucose
<input type="radio"/>	Oral chlorpromazine
<input type="radio"/>	Oral diazepam
<input type="radio"/>	Oral propranolol



IV glucose **This is the correct answer**

The history of three recent attacks of acute anxiety and abdominal pain coupled with starting the oral contraceptive pill raises the possibility of acute intermittent porphyria. Use of IV or oral glucose during an attack can lead to more rapid resolution of symptoms, and that would be the favoured approach here. Glucose inhibits haem synthesis, thereby reducing the production of porphyrin precursors. The UK guidelines recommend 5% glucose in 0.9% saline, initially at a rate of 2L/24h. You should avoid IV glucose in water solutions (e.g. dextrose 5%) as those can aggravate hyponatraemia.

The contraceptive pill should be withdrawn if possible.

There is no indication of acute sepsis, so use of IV antibiotics is inappropriate.

Phenothiazines may be used for restlessness, nausea and anxiety, and beta blockers have a role in the management of sympathetic activation.

It is glucose however that will have the most impact in shortening the duration and severity of symptoms.

### Question 173 of 206

#### Core Questions

A 45-year-old, obese, Afro-Caribbean woman presented with unexplained confusion, shortness of breath, cold and pain in her fingers and toes.

She is usually fit and well and had only a transient gastrointestinal upset few weeks ago, after which she has felt increasingly tired with worsening confusion. She had no regular medications, did not smoke or use excessive amounts of alcohol. She has returned from a two-day trip to Malaysia yesterday.

On examination, she was mildly confused, looked generally pale with cold peripheries and very pale nail folds. She was afebrile, mildly tachycardic and tachypnoeic with normal heart sounds and bibasal crepitations on chest auscultation. She had no focal neurological deficit or cranial nerve palsy but during examination, she developed a one-minute seizure involving the right side of her body.

Her chest x ray showed bilateral peripheral patchy parenchymal opacities and routine bloods showed:

<b>Sodium</b>	137 mmol/L	(137-144)
<b>Potassium</b>	5.8 mmol/L	(3.5-4.9)
<b>Creatinine</b>	110 µmol/L	(60-110)
<b>Urea</b>	7.1 mmol/L	(2.5-7.5)
<b>Albumin</b>	36 g/L	(37-49)
<b>Total bilirubin</b>	28 µmol/L	(1-22)
<b>Alk.phosphatase</b>	77 IU/L	(30-110)
<b>ALT</b>	14 IU/L	(5-40)
<b>LDH</b>	450 IU/L	(672)
<b>CRP</b>	8 mg/L	(<5)
<b>Hb</b>	79 g/L	(130-180)
<b>Haematocrit</b>	25%	
<b>WBC</b>	$11.6 \times 10^9/L$	(4-11)
<b>Platelets</b>	$20 \times 10^9/L$	(150-400)

<b>MCV</b>	93 fL	(80-96)
<b>Prothrombin time</b>	14.2 seconds	(11.5-15.5)
<b>INR</b>	1.1	<1.4
<b>APTT</b>	21.2 seconds	(30-40)

Peripheral smear shows fragmented schistocytes and an elevated reticulocyte count.

Which is the most likely cause of this patient's neurological presentation?

(Please select 1 option)

<input type="radio"/>	Cerebral malaria
<input type="radio"/>	Cerebral venous sinuses thrombosis
<input type="radio"/>	Haemolytic uraemic syndrome
<input type="radio"/>	Intracranial haemorrhage due to essential thrombocytopenia
<input type="radio"/>	Thrombotic thrombocytopenic purpura (TTP)
<input checked="" type="radio"/>	Thrombotic thrombocytopenic purpura (TTP) <b>Correct</b>

TTP is a clinical diagnosis and potential diagnosis in any patient with anaemia and thrombocytopenia; 95% of cases are fatal if left untreated.

Symptoms are usually non-specific. Renal and neurological dysfunctions are the main complications.

Examination of the peripheral smear is critical and shows evidence of microangiopathic haemolytic anaemia with fragmented RBCs (schistocytes) and thrombocytopenia. An urgent haematological consultation is recommended for suspected cases. Plasma exchange therapy is the mainstay of treatment.

A pentad of clinical features which characterise the disease are:

- Microangiopathic haemolytic anaemia. The peripheral smear shows microangiopathic haemolysis as evidenced by the presence of schistocytes
- Thrombocytopenia with purpura
- Acute renal insufficiency (usually less marked in TTP than in haemolytic uraemic syndrome)
- Neurological abnormalities (usually more marked in TTP than in haemolytic uraemic syndrome) Neurological manifestations are present in most patients, and range from confusion and severe headache, to focal neurological abnormalities, seizures and coma
- Fever.

Not all of the above may be present.

Other features are:

- Purpura, ecchymosis, and menorrhagia due to thrombocytopenia may also be seen in 20% of cases
- Peripheral digit ischaemic syndrome
- Nonocclusive mesenteric ischaemia
- Adult respiratory distress syndrome (ARDS).

Additional laboratory findings:

- The reticulocyte count is generally elevated
- Lactate dehydrogenase and bilirubin are often elevated as markers of haemolysis
- Direct Coombs' test should be negative to rule out autoimmune haemolytic anaemia
- Assays have been developed to measure von Willebrand factor cleaving enzyme (ADAMTS-13) activity. ADAMTS-13 activity can be low, and inhibitors to its activity can often be demonstrated in patients with TTP.

Cerebral malaria is an important differential diagnosis in travellers to the endemic areas and who present with decreased Glasgow coma score (GCS) and history of fevers, but the incubation period is usually 7 to 14 days. In this case, the patient developed symptoms gradually, and prior to her travel.

A history of fevers would strongly suggest the possibility of malaria although fever may also be present in TTP, sepsis, and disseminated intravascular coagulation (DIC), and all can give a similar laboratory picture. TTP in this clinical scenario would be the first on the differential list.

Cerebral venous sinuses thrombosis clinically may present as headache, focal neurological deficit, seizures and decreased level of GCS but pathogenesis is usually associated with prothrombotic conditions (with thrombocytosis being more likely rather than thrombocytopenia).

The pathogenesis of neurological disturbances in TTP is formation of microthrombi in microcirculation.

Haemolytic uraemic syndrome is the main differential in thrombocytopenia and haemolytic anaemia but this presents with more marked renal failure and neurological complications occur less frequently.

This is clearly not essential thrombocytopenia, which, as the definition says, affects only megakaryocytic lineage. In this clinical scenario, there is laboratory evidence of haemolytic anaemia.

### Question 174 of 206

A 20-year-old male is referred to the haematology clinic with a raised platelet count of  $600 \times 10^9/L$ . Blood film demonstrates target cells and Howell-Jolly bodies.

On further questioning, the patient reveals that he was involved in a road traffic accident at the age of 12 and required emergency abdominal surgery. Physical examination demonstrates a left subcostal scar with no evidence of organomegaly.

Which is the next course of action?

(Please select 1 option)

<input type="radio"/>	Antimicrobial prophylaxis daily
<input type="radio"/>	Antimicrobial prophylaxis prior to invasive procedures only
<input type="radio"/>	Regular outpatient follow-up with no intervention
<input type="radio"/>	Vaccination
<input type="radio"/>	Vaccination and commence antimicrobial prophylaxis

<input checked="" type="radio"/>	Vaccination and commence antimicrobial prophylaxis <b>Correct</b>
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All patients who have undergone splenectomy for any reason and those with functional hyposplenism should receive pneumococcal immunisation, and patients not previously immunised should receive *Haemophilus influenzae* type b vaccine and meningococcal Group C conjugate vaccine, together with influenza immunisation.

Lifelong prophylactic antibiotics (penicillin V or macrolides if penicillin allergic) are still recommended.

### Question 175 of 206

A 30-year-old gentleman presents to the Emergency Department with a three-day history of tiredness and fever. On the day of presentation he also noticed bruising over his hands and feet and that he has not been passing water for the previous day.

Blood investigations show a creatinine of 560  $\mu\text{mol/L}$ , a haemoglobin of 70 g/L with prominent red cell fragments on blood film, and a platelet count of  $10 \times 10^9/\text{L}$ . The patient reports no prior illness.

Which of the following is the established treatment for this condition?

(Please select 1 option)

<input type="radio"/>	Anti-complement therapy with eculizumab
<input type="radio"/>	Dialysis
<input type="radio"/>	Fresh frozen plasma
<input type="radio"/>	Plasma exchange
<input type="radio"/>	Plasma exchange and dialysis



Plasma exchange and dialysis **This is the correct answer**

The presentation is typical of diarrhoea negative (D- or atypical) haemolytic uraemic syndrome (HUS), often difficult to discern from thrombotic thrombocytopenic purpura (TTP) except for the prominent presence of oliguria/uraemia. Plasma exchange and dialysis are established supportive therapies for HUS.

Diarrhoea positive (D+) HUS, associated typically with verotoxin-induced bloody diarrhoea, is treated with supportive care whereas negative (D-) HUS, not typically associated with bloody diarrhoea but sometimes associated with multisystem symptoms similar to TTP, should be urgently treated with plasmapheresis.

Increasingly, the role of complement defects in atypical HUS is being defined and use of the complement inhibitor, eculizumab, appears useful in these instances.

### Question 176 of 206



A 70-year-old lady presents to the Emergency Department at 2 am complaining of acute onset of severe bilateral headache, right upper and lower limb weakness, nausea, vomiting, and breathlessness. Computed tomography of the head shows no intracranial pathology.

Blood investigations show a haemoglobin of 50 g/L, a platelet count of  $2 \times 10^9/L$  and no renal impairment. Clotting screen, including fibrinogen, is normal. Blood film examination shows extensive red cell fragments and confirms genuine thrombocytopenia.

Which is the most probable underlying pathophysiology?

(Please select 1 option)

<input checked="" type="radio"/>	Acute ischaemic stroke
<input type="radio"/>	Disseminated intravascular coagulation (DIC)
<input type="radio"/>	Evans syndrome
<input type="radio"/>	Haemolytic uraemic syndrome (HUS)

	Thrombotic thrombocytopenic purpura (TTP)
	Thrombotic thrombocytopenic purpura (TTP) <b>This is the correct answer</b>

Thrombotic thrombocytopenic purpura (TTP) is a medical emergency, originally defined as a classic pentad of:

- thrombocytopenia
- MAHA (microangiopathic haemolytic anaemia)
- neurological signs which tend to be fluctuating
- renal impairment, and
- fever.

Fever and renal impairment, although described as part of the classical pentad, are usually absent in the acute presentation.

Evans syndrome, the combination of autoimmune haemolytic anaemia and thrombocytopenia only, does not cause multisystem symptoms, and DIC is excluded by the normal clotting screen and fibrinogen.

Although an ischaemic stroke is evident in this case, it is the platelet activation and resulting ischaemia from the TTP which is the underlying pathophysiological mechanism in play rather than a primary CVA.

Thrombotic thrombocytopenic purpura should be considered a medical emergency, and the initial diagnosis should be made on clinical history, examination and routine laboratory testing and blood film. To avoid early mortality, treatment with plasma exchange should be commenced on the day of the presentation as soon as possible.

### Question 177 of 206

A 35-year-old lady diagnosed with Hodgkin disease treated with autologous stem cell transplantation has now relapsed two years post-transplant. She is started on salvage chemotherapy prior to possible allogeneic bone marrow transplantation.

She has cytotoxic related cytopenias, including anaemia (70 g/L) and thrombocytopenia ( $10 \times 10^9/L$ ) and is symptomatic, with lethargy and bruising, thus requiring regular blood product support.

Which is the most appropriate blood product for this patient?

(Please select 1 option)

<input type="radio"/>	Irradiate prior to allogeneic bone marrow transplant only
<input type="radio"/>	Irradiated platelet concentrates only
<input type="radio"/>	Irradiated red cell and platelet concentrates
<input type="radio"/>	Irradiated red cell concentrates only
<input type="radio"/>	Standard red cell and platelet concentrates

<input checked="" type="radio"/>	Irradiated red cell and platelet concentrates <b>This is the correct answer</b>
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The patient has several indications for irradiated blood product administration. Transfusion associated GvHD has been reported in Hodgkin disease and irradiation for all products is suggested lifelong in Hodgkin lymphoma. Autologous bone marrow transplant recipients should receive irradiated products for up to six months from start of conditioning. As this patient has a history of Hodgkin lymphoma, lifelong irradiated blood product administration is the correct choice.

Transfusion associated GvHD is caused by white blood cells contaminating the transfused products acting against the recipient bone marrow; irradiation eliminates these white blood cells. Blood product irradiation is used to eliminate the risk of transfusion related graft versus host disease, a universally fatal complication of blood transfusion. It is worthwhile to review the indicated instances where it is imperative that irradiated blood products are used.

### Question 178 of 206

#### Core Questions

A 10-year-old boy presents to his GP with a three-day history of malaise, fever, headache, myalgia, and nausea. The symptoms resolve with conservative treatment but within a week

the boy presents again, this time to the Emergency Department with pallor, fatigue, and breathlessness.

His blood investigations show a haemoglobin of 30 g/L, a platelet count of  $15 \times 10^9/\text{L}$ , and a white cell count of  $2 \times 10^9/\text{L}$ .

Parvovirus B19 (erythrovirus) specific IgM by ELISA and viral DNA by PCR were both detected in high titre.

Which is the underlying mechanism of this complication?

(Please select 1 option)

<input type="radio"/>	Aplastic anaemia due to direct cytotoxic effect on erythropoiesis
<input type="radio"/>	Cytopenias due to consumption
<input type="radio"/>	Molecular mimicry by virus antigen
<input type="radio"/>	Nutritional deficiency
<input type="radio"/>	Raised cytokine

<input checked="" type="radio"/>	Aplastic anaemia due to direct cytotoxic effect on erythropoiesis <b>This is the correct answer</b>
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It is known that parvovirus B19 plays a distinctive role in aplastic crises due to its direct cytotoxic effect on haemopoietic progenitors. The cellular receptor responsive for the entry of the virus is an antigen of the group blood P, which is present not only on erythrocytes and erythroblasts but also on megakaryocytes and granulocytes, resulting in the progenitors being killed by the cytotoxic effect of the virus load and the reticulocytes being cleared by the reticuloendothelial system.

The patients most at risk are those already having a bone marrow disorder resulting in decreased or functionally abnormal haemoglobin production, such as haemoglobinopathies.

### Question 179 of 206

A 70-year-old lady is referred to haematology for investigation of an anaemia of 90 g/L coupled with thrombocytopenia of  $50 \times 10^9/L$ . She had been complaining of breathlessness at rest for the past two months.

On physical examination, she has massive splenomegaly down to her right iliac fossa. Blood film examination shows anaemia with teardrop poikilocytosis with no blasts evident. Bone marrow aspiration is unsuccessful, but a trephine biopsy shows infiltration by silver stain positive collagenous strands.

Which is the most probable underlying haematological diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Essential thrombocytaemia
<input type="radio"/>	Myelodysplasia
<input type="radio"/>	Myelofibrosis
<input type="radio"/>	Polycythaemia

<input checked="" type="radio"/>	Myelofibrosis <b>This is the correct answer</b>
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Primary myelofibrosis is a disorder in which normal bone marrow tissue is gradually replaced with a fibrous scar-like material. Over time this leads to progressive bone marrow failure. It is almost always accompanied by significant splenomegaly and is JAK2 mutation-positive in about 50% of cases. It is generally incurable, although bone marrow transplantation and JAK2 inhibitors have a role in younger patients.

Acute myeloid leukaemia would be evidenced by circulating blasts, whereas polycythaemia would show an increased red cell mass.

Essential thrombocytaemia is characterised by severely elevated platelet counts, whereas myelodysplasia would show cytopenias but no marrow infiltration by fibrous material.

### Question 180 of 206

A 35-year-old male, morbidly obese with a BMI of  $40 \text{ kg/m}^2$ , is assessed by a multi-disciplinary team prior to undergoing bariatric surgery with gastric bypass (Roux-en-Y procedure). Assessment of nutritional status and vitamins pre-operatively shows no deficiency.

Six months after the procedure on routine follow-up it is noted the patient has a haemoglobin of  $80 \text{ g/L}$  with macrocytosis. The patient admits that he has not been fully compliant with the supplementation suggested by his caring team.

Which is the most probable nutritional deficiency accounting for this presentation?

(Please select 1 option)

<input type="radio"/>	Vitamin A
<input type="radio"/>	Vitamin B12 deficiency
<input type="radio"/>	Vitamin D
<input type="radio"/>	Selenium
<input type="radio"/>	Thiamine

<input checked="" type="radio"/>	Vitamin B12 deficiency This is the correct answer
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Bariatric patients are at an increased risk of developing vitamin B12 deficiency because their digestive tracts have been altered in such a way as to interfere with the natural absorption of this vitamin. In patients who have had gastric bypass surgery, most of the stomach and duodenum are bypassed, limiting the breakdown of vitamin B12 and its subsequent binding with intrinsic factor.

Deficiencies of folate, zinc, vitamin D, calcium and thiamine have also been observed in those undergoing bariatric surgery, but would not solely account for the clinical presentation described above as they would present with skin rashes (zinc), beriberi and Wernicke-Korsakoff syndrome (thiamine) or osteomalacia (vitamin D).

### Question 181 of 206

A 32-year-old lady presents to her GP with a one-week history of lesions over her shins. They are painful, red, and about 3 cm in diameter, noted by her GP to be over the extensor aspect of the legs only.

Her only medical history of note is that she has been commenced on the oral contraceptive pill about a month prior to presentation to control irregular menses.

What is the most probable underlying pathophysiology?

(Please select 1 option)

<input type="radio"/>	Deep vein thrombosis
<input type="radio"/>	Erysipelas
<input type="radio"/>	Erythema nodosum
<input type="radio"/>	Superficial thrombophlebitis
<input type="radio"/>	Urticaria

<input checked="" type="radio"/>	Erythema nodosum This is the correct answer
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The presentation is typical of the nodular lesions of erythema nodosum, made all the more probable by a known inciting factor in the oral contraceptive pill. Erythema nodosum (EN) is an acute, nodular, erythematous eruption that usually is limited to the extensor aspects of the lower legs. It is presumed to be a hypersensitivity reaction in the subcutaneous panniculus

and may occur in association with several systemic diseases, infections or drug therapies, as well as being idiopathic.

Causes include:

- tuberculosis
- inflammatory bowel disease
- streptococcal infection
- pregnancy
- drugs (penicillin, sulphonamides, oral contraceptive pill), and
- sarcoidosis.

Erysipelas and superficial thrombophlebitis tend to cause less discrete, more extensive lesions. Deep vein thrombosis would usually be unilateral swelling of the lower limb, which can be accompanied by pain. Urticaria causes characteristic wheals and flares not present in this case.

### Question 182 of 206

#### Core Questions

A 55-year-old lady is referred to haematology with a monoclonal paraprotein reported on serum protein electrophoresis, together with an elevated erythrocyte sedimentation rate and haemoglobin of 80 g/L on tests performed by her GP for myalgia.

On further examination by the haematology team, she is discovered to have several lytic lesions on her skeletal survey, a calcium of 2.8 mmol/L, bone marrow plasma cell infiltrate amounting to 41% and normal renal function.

What is the most probable underlying diagnosis?

(Please select 1 option)

<input type="radio"/>	Asymptomatic myeloma
<input type="radio"/>	Hypoparathyroidism
<input type="radio"/>	Monoclonal gammopathy of uncertain significance (MGUS)
<input type="radio"/>	Multiple myeloma
<input type="radio"/>	Osteoporosis

<input checked="" type="radio"/>	Multiple myeloma <b>This is the correct answer</b>
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This lady has active myeloma with evidence of myeloma ROTI (myeloma-related organ and tissue impairment), with development of anaemia, hypercalcaemia, bone lesions and a plasma cell infiltrate of her bone marrow above 30%.

MGUS is the presence of low-level paraprotein with no end organ damage. Osteoporosis and hypoparathyroidism do not fit with the biochemical profile described or the clinical presentation. The development of myeloma ROTI excludes asymptomatic myeloma as a diagnosis.

Multiple myeloma may present insidiously with just a monoclonal paraprotein and normochromic normocytic anaemia, although hypercalcaemia, bone lesions and renal impairment should raise red flags about an underlying plasma cell disorder.

### Question 183 of 206

A 60-year-old gentleman is referred to haematology with an elevated calcium level at 2.9 mmol/L, a normochromic normocytic anaemia of 85 g/L, and a serum protein electrophoresis showing a monoclonal paraprotein quantified at 25 g/L. Over the past week, he has also complained of severe back pain in the lumbosacral region radiating to his groin, with numbness of both lower limbs.

Which would be the next appropriate diagnostic investigation in this case?

(Please select 1 option)

<input type="radio"/>	Bone marrow examination
<input type="radio"/>	Magnetic resonance imaging of the whole spine
<input type="radio"/>	PET-CT imaging
<input type="radio"/>	Serum free light chains

<input type="radio"/>	Skeletal survey
<input checked="" type="radio"/>	Magnetic resonance imaging of the whole spine <b>This is the correct answer</b>

Tests to establish the diagnosis of multiple myeloma include:

- bone marrow aspiration and trephine for plasma cell phenotyping
- immunofixation of serum and urine, and
- skeletal survey.

Serum free light chain assay is used in oligo- or non-secretory disease.

Although PET-CT is developing its own niche in imaging myelomatous deposits, in this case, urgent magnetic resonance imaging to assess bone disease with possible spinal cord compression is the most urgent investigation.

### Question 184 of 206

A 3-year-old child is admitted to hospital due to loose bowel motions with no fresh or altered blood, fever, and vomiting. *Escherichia coli* subtype O157:H7 is cultured from his stool. With adequate resuscitation, he makes an uneventful recovery and is discharged home after seven days.

He presents again 10 days from initial presentation with bloody diarrhoea and collapse. His renal function tests are severely deranged, his clotting screen is normal but blood film examination shows severe thrombocytopenia with evidence of microangiopathic anaemia. Coombs' test and C-reactive protein are both negative.

Which is the most probable underlying complication?

(Please select 1 option)

<input type="radio"/>	Autoimmune haemolytic anaemia (AIHA)
<input type="radio"/>	Disseminated intravascular coagulation (DIC)

<input type="radio"/>	Haemolytic uraemic syndrome (HUS) due to VTEC <i>E. coli</i>
<input type="radio"/>	Septicaemia
<input type="radio"/>	Thrombotic thrombocytopenic purpura (TTP)

<input checked="" type="radio"/>	Haemolytic uraemic syndrome (HUS) due to VTEC <i>E. coli</i> This is the correct answer
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The initial presentation with diarrhoea with culture positive *E. coli* O157-H7 should lead one to consider HUS as the complication. Negative Coombs' test is against AIHA, whereas TTP would show several red cell fragments and neurological complications.

DIC is excluded by the normal clotting screen and septicaemia is improbable seeing the normal inflammatory markers.

HUS due to VTEC *E. coli* is the most probable diagnosis.

Haemolytic uraemic syndrome (HUS) is a triad of:

- microangiopathic haemolytic anaemia (Coombs' test negative)
- thrombocytopenia, and
- acute renal failure.

Typical HUS is most commonly associated with *Escherichia coli* with somatic (O) antigen 157 and flagella (H) antigen 7, hence the designation O157:H7. It produces a toxin called Shiga toxin or verotoxin. General management includes appropriate fluid and electrolyte management, antihypertensive therapy and dialysis where required.

### Question 185 of 206

A 20-year-old lady is referred after complaining of a longstanding history of heavy menstrual bleeding. On further history taking it is elucidated that she had sustained bleeding when she had two molar teeth extracted at the age of 14 and she gets repeated nosebleeds with no preceding trauma.

What is the most probable clotting deficiency this patient suffers from?

(Please select 1 option)

<input type="radio"/>	Acquired von Willebrand disease
<input type="radio"/>	Factor XII deficiency
<input type="radio"/>	Haemophilia A
<input type="radio"/>	Haemophilia B
<input type="radio"/>	von Willebrand disease, type 1

<input checked="" type="radio"/>	von Willebrand disease, type 1 <b>This is the correct answer</b>
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Haemophilia A and haemophilia B present with significant bleeding in infancy due to lack of the relevant factors (factor VIII and factor IX). Factor XII deficiency has no clinical sequelae.

Acquired von Willebrand disease tends to occur later in life and is associated with thyroid and endocrine dysfunction. The bleeding post trauma aged 14 with ongoing history until 20 is against the development of acute antibodies in acquired von Willebrand disease.

Type 1 von Willebrand disease is the most common subtype of von Willebrand disease, with the typical mild bleeding, menorrhagia, and bleeding post procedure described above. von Willebrand disease (vWD) is a relatively common inherited, genetically and clinically heterogeneous clotting disorder caused by a deficiency or dysfunction of the protein termed von Willebrand factor (vWF). Consequently, defective vWF interaction between platelets and the vessel wall impairs primary haemostasis. It is diagnosed by taking a detailed clotting history, together with von Willebrand factor assay, ristocetin cofactor activity, PT, aPTT, and factor VIII activity, using genetic studies in difficult complex cases.

### Question 186 of 206

A 14-year-old girl is referred to haematology after being investigated for heavy menstrual bleeding and recurrent epistaxis by her gynaecologist. Clotting tests show a normal PT, but mildly prolonged aPTT. Further tests ordered by the haematologist show decreased levels of factor VIII and von Willebrand factor.

She is diagnosed with type 1 von Willebrand disease. Her mother has the same pathology and her two other sisters are unaffected.

What is the method of inheritance of this common clotting disorder?

(Please select 1 option)

<input type="radio"/>	Acquired
<input type="radio"/>	Autosomal dominant
<input type="radio"/>	Autosomal dominant with variable penetrance
<input type="radio"/>	Autosomal recessive
<input type="radio"/>	De novo acquisition

<input checked="" type="radio"/>	Autosomal dominant with variable penetrance <b>This is the correct answer</b>
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von Willebrand disease (VWD) is divided into three major categories:

- Type I - partial quantitative deficiency
- Type II - qualitative deficiency
- Type III - total deficiency.

VWD type II is further divided into four variants (IIA, IIB, IIN, IIM) based on characteristics of dysfunctional vWF. These categories correspond to distinct molecular mechanisms, with corresponding clinical features and therapeutic recommendations.

Type I vWD is the most common form of the disease and is inherited in an autosomal dominant manner, with variable penetrance being commonly observed. Von Willebrand disease is estimated to affect 1 in 100 to 10,000 individuals. Because people with mild signs and symptoms do not usually come to medical attention, it is thought that this condition is underdiagnosed, also taking into consideration the variable penetrance of the inheritance mechanism.

The inheritance pattern of type II is autosomal dominant, whereas in type III it is autosomal recessive.

### Question 187 of 206

A 55-year-old lady presents to the Emergency Department with a 2-week history of lethargy, bruising, breathlessness at rest. Over the past 24 hours, she also developed a fever of 39°C.

Physical examination shows pallor and ecchymosis over her back, together with 3 cm hepatomegaly. Blood investigations show an elevated white cell count at  $101 \times 10^9/L$ , haemoglobin of 54 g/L, platelet count of  $10 \times 10^9/L$  and a C-reactive protein of 210 mg/dL. Blood film examination shows a prominent leukocytosis with big cells with a high nucleocytoplasmic ratio with rare Auer rods.

What is the most probable underlying pathology?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Chronic myeloid leukaemia
<input type="radio"/>	Follicular lymphoma
<input type="radio"/>	Myelofibrosis
<input type="radio"/>	Myelodysplasia

<input checked="" type="radio"/>	Acute myeloid leukaemia This is the correct answer
----------------------------------	--

The acute onset of symptoms, all related to abrupt onset of anaemia, thrombocytopenia and immunocompromise from neutropenia and presence of non-functional blast cells point to an acute malignancy. Blasts are not present in chronic myeloid leukaemia, unless in accelerated or blast phase and basophilia is usually present.

Myelofibrosis would show prominent red cell morphology defects and splenomegaly.

Follicular lymphoma would consist of small to medium circulating cells and no Auer rods.

Although myelodysplasia is a diagnostic possibility, the presence of blast cells signifies transformation to acute myeloid leukaemia.

The presence of bone marrow failure, with circulating myeloid blasts, all developing over a short period of time with no antecedent symptoms points towards acute myeloid leukaemia.

Treatment involves resuscitation, antimicrobial cover of sepsis and institution of appropriate cytotoxic agents if indicated after characterization of AML using flow cytometry, depending on the performance status of the patient and after discussion of prognosis with the patient.

### Question 188 of 206

A 30-year-old lady presents to the Emergency Department with a 2-week history of bruising, accompanied by bleeding from her gums and nose. She has no prior medical history, was not admitted to hospital recently and takes no medication.

Physical examination shows extensive purpura over her extremities, together with wet blisters on her tongue and gums. Blood investigations show a platelet count of  $1 \times 10^9/L$ , with normal white cell count, haemoglobin and clotting studies.

Which is the most probable diagnosis in this case?

(Please select 1 option)

<input type="radio"/>	Autoimmune haemolytic anaemia (AIHA)
<input type="radio"/>	Disseminated intravascular coagulation (DIC)
<input type="radio"/>	Immune thrombocytopenia (ITP)
<input type="radio"/>	Pseudo-thrombocytopenia
<input type="radio"/>	Thrombotic thrombocytopenic purpura (TTP)

<input checked="" type="radio"/>	Immune thrombocytopenia (ITP) This is the correct answer
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The diagnosis of ITP is made in the presence of isolated thrombocytopenia with normal bone marrow and with no other identifiable cause for thrombocytopenia.

AIHA and TTP would show manifest anaemia and haemolysis, not present here, whereas DIC would show an overtly abnormal clotting test profile.

Pseudo-thrombocytopenia results from platelet clumping in the presence of ethylene-diamine-tetra-acetic acid (EDTA) but has no clinical manifestations in vivo.

### Question 189 of 206

A 30-year-old lady presents to the Emergency Department with a 1-week history of bruising, accompanied by bleeding from her gums and nose. She has no prior medical history, was not admitted to hospital, and takes no medication.

Physical examination shows extensive purpura over her extremities, together with wet blisters on her tongue and gums. Blood investigations show a platelet count of  $1 \times 10^9/L$ , with normal white cell count, haemoglobin and clotting studies. Bone marrow examination shows normal marrow morphology and the patient is diagnosed with ITP.

On the second day of hospital admission the patient complains of severe headache and weakness of the right side of her body. Computed tomography shows an extensive left sided intra-cerebral bleed.

What is the most appropriate treatment for ITP in this case?

(Please select 1 option)

<input type="radio"/>	Combination of IV immunoglobulin, corticosteroids, TPO agent and platelet transfusion
<input type="radio"/>	IV corticosteroids only
<input type="radio"/>	IV immunoglobulin only
<input type="radio"/>	Platelet transfusion
<input type="radio"/>	TPO agent only (thrombopoietin agonist)

<input checked="" type="radio"/>	Combination of IV immunoglobulin, corticosteroids, TPO agent and platelet transfusion <b>Correct</b>
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The management of acute ITP with a life threatening bleed is poorly characterised in evidence-based trials due to the ethical considerations. Seeing the patient has a severe intracerebral bleed with probable neurological sequelae, quick normalisation of platelet count is imperative, thus the use of a combination of steroids, IVIg, TPO agonist and platelet concentrate transfusion (in itself not usually efficacious in management of ITP) is imperative.

Splenectomy, immunosuppressive agents and the above agents alone all have a role to play in the management of chronic ITP. It is vitally important to recognise a life-threatening bleed early and manage it with all the treatment modalities at hand to normalise the platelet count as expeditiously as possible to curtail bleeding and consequent morbidity and mortality.

### Question 190 of 206

A 35-year-old gentleman presents complaining of a 6-month history of weight loss and tiredness. On further questioning, the patient also reports night sweats.

Physical examination shows hepatosplenomegaly but no lymphadenopathy. Blood film examination shows a considerable increase in the white cell count, with all stages of myeloid maturation present, together with thrombocytosis, basophilia, and eosinophilia.

Which of the following haematological conditions is most consistent with this patient's presentation?

(Please select 1 option)

<input type="radio"/>	Acute lymphoblastic leukaemia
<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Chronic myeloid leukaemia
<input type="radio"/>	Hodgkin lymphoma
<input type="radio"/>	Leukaemoid reaction



Chronic myeloid leukaemia **This is the correct answer**

At the time of diagnosis, most CML patients (85% to 90%) are in the chronic phase of CML (the other phases are accelerated and blast stages). The diagnosis is suggested by an incidental laboratory detection of an increased WBC count. When they are present, symptoms in CML patients generally relate to a hypermetabolic state, excessive leukocyte count, or splenic enlargement, and include fatigue, night sweats, weight loss and abdominal fullness related to organomegaly.

The most characteristic laboratory feature of CML in the chronic phase is an increase in WBC count, with all stages of maturation present. Accompanying the leukocytosis may be an increased platelet count and an increase in the number of basophils and eosinophils in the peripheral blood, as well as in the bone marrow. Definitive diagnosis is confirmed via the presence of the bcr-abl transcript, known as the Philadelphia chromosome.

#### Reference:

#### Question 191 of 206

What is the approximate incidence of forming pigment gallstones in patients with sickle cell disease?

(Please select 1 option)



20%



30%



50%



80%



90%

<input checked="" type="radio"/>	50% This is the correct answer
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Patients with haemolytic disorders such as sickle cell disease and hereditary spherocytosis have an approximately 50% incidence of forming pigment gallstones.

Black pigment gallstones are common in sickle cell disease and are due to an increase in bilirubin excretion. Their small size allows migration into the common bile duct causing low-grade obstruction typically leading to hyperbilirubinaemia rather than bile duct dilatation. In view of the high incidence of gallstones with such conditions cholecystectomy is suggested for patients with sickle cell disease if abdominal surgery is being performed for other reasons.

### Question 192 of 206

A 27-year-old woman with a family history of bleeding disorder comes to the obstetric clinic for review. She is completely well, but her maternal uncle and brother suffer from bleeding into joints and after tooth extractions. She is 20 weeks pregnant with her first child, which has been confirmed as male on ultrasound scan. The pregnancy has been unremarkable so far.

Routine blood testing is normal apart from her activated partial thromboplastin time (APTT), which is prolonged at 55 seconds (25-40).

What is the chance of her child suffering from the bleeding disorder?

(Please select 1 option)

<input type="radio"/>	0%
<input type="radio"/>	25%
<input type="radio"/>	33%
<input type="radio"/>	50%
<input type="radio"/>	100%

<input checked="" type="radio"/>	50% This is the correct answer
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The inheritance pattern here suggests an X-linked recessive bleeding disorder and therefore raises the possibility of haemophilia A. Although women who carry one copy of the abnormal gene do not generally suffer from increased bleeding tendency, there may be biochemical evidence with prolongation of the APTT. Because the value here is outside the normal range, it is likely she carries the gene for haemophilia A. She has a 1 in 2 chance of passing the gene on to a male child. Because it is X-linked, the child would be affected if he inherited one copy of the gene.

0% represents the approximate percentage chance of female offspring suffering from increased bleeding tendency. Case reports do exist that female haemophilia carriers do occasionally suffer from increased bleeding risk.

If the APTT was not known, then we would assume a 50% chance of her carrying the abnormal gene, giving a 25% chance of her male child inheriting the condition.

### Question 193 of 206

A 22-year-old woman presents to the haematology clinic for review. She has been referred by her GP after a significant bleeding episode at the dentist following a wisdom tooth extraction. She tells you that her uncle and sister have also had problems with bleeding at the dentist in the past.

Routine blood screening has been entirely normal apart from mild iron deficiency anaemia and a prolonged activated partial thromboplastin time (APTT) of 58 seconds (25-40). Clinical examination in the clinic is entirely normal.

Which is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Factor X deficiency
<input type="radio"/>	Factor XI deficiency
<input type="radio"/>	Haemophilia A

<input type="radio"/>	Haemophilia B
<input type="radio"/>	Von Willebrand disease
<input checked="" type="radio"/>	Von Willebrand disease <b>This is the correct answer</b>

Von Willebrand disease (VWD) is the most likely diagnosis here. VWD type 1 makes up 60-80% of cases and is associated with mild bleeding only. It is inherited in an autosomal dominant fashion. It is associated with a quantitative reduction of between 19% and 45% of VW factor (VWF). Type 2 is associated with a qualitative defect in VWF, and bleeding tendency varies between patients. Type 3 is autosomal recessive, associated with much more severe bleeding, and with very low/undetectable levels of VWF.

DDAVP is the initial treatment of choice for patients with VWD type 1. Other therapies such as factor VIII concentrates containing VWF are not usually required.

Haemophilia A and B are possible alternative diagnoses, although they are inherited in an X-linked recessive fashion, and as such females are not normally affected (although APTT may be prolonged in asymptomatic carriers).

Although factor XI deficiency (haemophilia C) results in prolongation of APTT, it only makes up 5% of bleeding disorders, as such it is very unlikely to be the cause here. Factor X deficiency is among the rarest of bleeding disorders, and both PT and APTT are prolonged in sufferers.

### Question 194 of 206

#### Core Questions

You are asked to review the lab results for a 71-year-old woman whose sample was sent in by the GP service. Clinical details report "swollen left leg".

Results are unremarkable apart from a potassium of 5.9 mmol/L (3.5-5.5) and a reduced activated partial thromboplastin time (APTT) of 16 seconds (25-40).

Which of the following is the most likely cause of the APTT result?

(Please select 1 option)

<input type="radio"/>	Elevated factor IX
<input type="radio"/>	Hyperfibrinogenemia
<input type="radio"/>	In-vitro clotting cascade activation
<input type="radio"/>	Protein C deficiency
<input type="radio"/>	Protein S deficiency
<input checked="" type="radio"/>	In-vitro clotting cascade activation <b>This is the correct answer</b>

The clues here include the fact that potassium is elevated and APTT is reduced, raising the possibility that this patient has proved difficult to bleed. Difficult phlebotomy, coupled with the fact that transport from a GP surgery can take a significant length of time, promotes in-vitro activation of the clotting cascade and drives a reduction in the APTT. The sample should, however, be repeated, because rarely a procoagulant state can exist leading to an actual rather than artefactual reduction in APTT.

Protein C and S deficiency do not promote a reduction in the APTT, but may, of course, be associated with hypercoagulability. Elevated factors XI, VIII, IX, II, and fibrinogen are recognised to lead to increased risk for venous thromboembolism and also lead to a reduction in APTT. It is thought that increased factor VIII activity is the commonest cause of reduced APTT, which also results in hypercoagulability.

### Question 195 of 206

A 72-year-old man comes to the haematology clinic for review. He has suffered increasing tiredness over the past four to six months, intermittent night sweats and abdominal fullness which is limiting his ability to finish a meal. As a consequence of this he has lost 4kg in weight.

He has a history of inferior myocardial infarction and asthma, for which he takes ramipril, indapamide, atorvastatin, aspirin and seretide.

On examination his BP is 145/85, pulse is 84 and regular. He looks pale and there is hepatosplenomegaly on abdominal palpation. His BMI is 23.

Investigations:

<b>Hb</b>	88 g/l (tear drop poikilocytes, nucleated red cells on film)	(135-180)
<b>WCC</b>	$7.2 \times 10^9/l$	(6-10)
<b>PLT</b>	$155 \times 10^9/l$	(150-400)
<b>Na</b>	136 mmol/l	(135-145)
<b>K</b>	4.0 mmol/l	(3.5-5.5)
<b>Cr</b>	112 $\mu\text{mol/l}$	(50-110)
<b>Glucose</b>	5.9 mmol/l	(<7.0)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Autoimmune haemolytic anaemia
<input type="radio"/>	B <sub>12</sub> deficiency
<input type="radio"/>	Chronic myeloid leukaemia
<input type="radio"/>	Myelofibrosis



Myelofibrosis **This is the correct answer**

The answer is myelofibrosis. Teardrop poikilocytes are said to be characteristic of myelofibrosis, and the anaemia with hepatosplenomegaly and gradually worsening symptoms of lethargy and night sweats over the past few months support the diagnosis. Platelet and white cell abnormalities are variably seen, with marked elevation in white cells seen in 10-15% of patients. Abnormalities in LFTs, particularly alkaline phosphatase, and urate with increased risk of gout are also seen. Treatment is tailored by risk stratification used to estimate overall survival, and by comorbidities which affect ability to tolerate chemotherapy intervention.

Acute myeloid leukaemia is incorrect as you would expect a significantly raised white cell count, with blasts present on blood film. Myelofibrosis can transform to AML, and therefore patients should be monitored for this.

Autoimmune haemolytic anaemia is usually associated with macrocytosis because of increased reticulocyte count, and hepatosplenomegaly would be less characteristic.

B<sub>12</sub> deficiency is associated with macrocytosis, and not with the blood film abnormalities seen here or hepatosplenomegaly.

CML can present with a similar clinical picture to that seen here, but tear drop poikilocytes are not characteristic.

### Question 196 of 206

#### Core Questions

A 19-year-old student in his first year at university presents to the Emergency Department complaining of severe sore throat.

He has no past medical history of note and takes no regular medications. On examination he is pyrexial 38.4°C, pulse is 85 and regular, and there is a severe pharyngitis with tonsillar exudates. He also has a fine macular rash over his upper body and there is mild tenderness on abdominal palpation in the left upper quadrant. Neck lymph nodes are enlarged.

Investigations:

<b>Hb</b>	140 g/l	135-180
<b>WCC</b>	9.2 x10 <sup>9</sup> /l (Lymphocytosis, >20% atypical lymphocytes seen on film)	6-10

<b>PLT</b>	355 x 10 <sup>9</sup> /l	150-400
<b>Na</b>	139 mmol/l	135-145
<b>K</b>	4.4 mmol/l	3.5-5.5
<b>Cr</b>	105 µmol/l	50-110
<b>Glucose</b>	5.2 mmol/l	<7.0
<b>CRP</b>	65 mg/dl	<10

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	B-cell lymphoma
<input type="radio"/>	CMV infection
<input type="radio"/>	Epstein-Barr infection
<input type="radio"/>	Hodgkin's lymphoma
<input type="radio"/>	Streptococcal tonsillitis
<input checked="" type="radio"/>	Epstein-Barr infection <b>This is the correct answer</b>

The answer is Epstein-Barr infection. The high fever with exudative pharyngitis, coupled with atypical lymphocytes fits well with a diagnosis of Epstein-Barr virus infectious

mononucleosis. Heterophile antibody testing is used to confirm the diagnosis, although in the early stages of the disease, (1st week), there is a 25% false negative rate. Management is supportive, and in the event, there is significant splenic tenderness/enlargement, the patient should be advised to avoid contact sports for up to eight weeks.

Given the short history and presence of atypical lymphocytes, both B cell and Hodgkin's lymphomas are unlikely as the underlying diagnosis. Streptococcal tonsillitis is not associated with atypical lymphocytes. CMV infection is associated with atypical lymphocytes but is much less likely than EBV to be associated with the severe tonsillitis/pharyngitis seen here.

### Question 197 of 206

#### Core Questions

A 52-year-old man is reviewed on the haematology ward. He presented to the Emergency Department with rapidly worsening lethargy, abdominal fullness and a tendency to bleed, he was diagnosed with acute lymphocytic leukaemia (ALL).

Which of the following is the translocation associated with the worst prognosis?

(Please select 1 option)

<input type="radio"/>	1:19
<input type="radio"/>	8:14
<input type="radio"/>	9:22
<input type="radio"/>	11:22
<input type="radio"/>	12:21

<input checked="" type="radio"/>	8:14 This is the correct answer
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The answer is 8:14. The 8:14 chromosomal translocation is associated with a particularly poor prognosis, and is found in approximately 1% of adults with ALL. The incidence of CNS

involvement is very high at the point of diagnosis, and median event free survival after chemotherapy is only two months.

The 9:22 translocation is known as the Philadelphia translocation, and is found in 30-50% of adults who are diagnosed with ALL, but is more classically associated with CML. In ALL it is associated with a much worse prognosis than in patients who are 9:22 translocation negative, with approximately a 50% reduced survival reported initially although this has improved with wider availability of tyrosine kinase inhibitors.

The 1:19 and 12:21 translocations are both associated with a favourable prognosis in ALL. 1:19 is associated with TCF3/PBX1 expression, (not normally found in lymphoid tissue), and 12:21 is the commonest translocation found in childhood ALL. Taken together they are associated with five-year survival of 85% or greater.

The 11:22 translocation is associated with a congenital syndrome characterised by mental retardation, craniofacial abnormalities and congenital heart disease, but not leukaemia.

### Question 198 of 206

A 70-year-old woman comes to the Emergency Department having taken an overdose of her bisoprolol which has been prescribed for hypertension and atrial fibrillation. Her husband passed away from cancer some 10 days ago, and she admits to being very lonely and depressed. She has a past history of ischaemic heart disease but is able to self-care and is independent.

She owns her own home and receives a workplace pension from her husband's contributions. There is a history of depression some 20 years earlier, but she has not taken medication for this in the past. Physical examination reveals bradycardia of 35 consistent with her overdose and a BP of 90/60, it is otherwise unremarkable.

Which of the points in her history is associated with the greatest risk of suicide?

(Please select 1 option)

<input type="radio"/>	Age 70
<input type="radio"/>	Chronic physical illness
<input type="radio"/>	Female sex
<input type="radio"/>	Previous history of depression

<input type="radio"/>	Recent bereavement
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<input checked="" type="radio"/>	Recent bereavement <b>This is the correct answer</b>
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The answer is her recent bereavement. The death of this patient's spouse has the greatest impact on her risk of suicide. During the first week after a bereavement, the standardised mortality ratio for women is 120 times the background rate, versus 90 times for men. Given the proximity to the event, (only 10 days earlier), close monitoring of this woman is indicated to prevent another suicide attempt.

Successful suicide is more common in males than females, although depression, chronic illness, and increasing age all impact negatively on risk. In this case, there are no signs of heart failure, implying her physical illness is relatively well managed, and the depression occurred some years earlier.

Family history has a strong impact on suicide risk, with a three-fold increased risk of suicide amongst women with a sibling who has successfully taken their own life, and a two-fold increase for men.

### Question 199 of 206

A 22-year-old man presents to the Emergency Department with severe bleeding around his gum line. He also has extensive bruising affecting his arms and legs, and petechial haemorrhages over his upper body. He has felt increasingly tired over the past month, so much so that now he can barely get out of bed.

Examination reveals a BP of 110/80, pulse is 89 and regular, he looks pale and you confirm the extensive bruising. There is splenomegaly on palpation of the abdomen. Bone marrow biopsy and cytogenetics are suggestive of acute promyelocytic leukaemia (APML).

Which of the following translocations is most likely to be present?

(Please select 1 option)

<input type="radio"/>	4:11
<input type="radio"/>	11:23

<input type="radio"/>	12:21
<input type="radio"/>	15:17
<input type="radio"/>	9:22

<input checked="" type="radio"/>	15:17 This is the correct answer
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The answer is 15:17. APL is characterised by the 15:17 translocation, which results in formation of the PML/RAR $\alpha$  gene on chromosome 15 and a RAR $\alpha$ /PML gene on chromosome 17. The PML gene under normal circumstances is thought to play a role in control of apoptosis, and it acts as a transcriptional co-activator with p53, a tumour suppressor gene. The fusion protein which is encoded for by the translocation functions as an aberrant retinoid receptor. This explains why treating with all-trans retinoic acid promotes cell differentiation and is an initial intervention of choice for the condition. APL often presents with clotting abnormalities, including disseminated intravascular coagulation (DIC).

4:11, 11:23, 12:21 and 9:22 are all translocations seen in acute lymphoblastic leukaemia, (ALL). The 4:11 translocation is associated with a particularly poor prognostic form of ALL, with CNS infiltration at the time of diagnosis.

The 9:22 translocation is the Philadelphia chromosome, seen in up to 30-50% of adults with ALL, and is associated with a poorer prognosis versus those who are Philadelphia chromosome negative. It is also commonly seen in cases of CML.

### Question 200 of 206

A 25-year-old male with a recent diagnosis of Hodgkin's lymphoma on treatment presents with tingling in his hands and fingers, as well as an intermittent "burning sensation" in his feet.

Bloods reveal:

<b>Na</b>	136 mmol/L	(135-145 mmol/L)
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<b>K</b>	4.6 mmol/L	(3.5-4.9 mmol/L)
<b>Cr</b>	119 µmol/L	(60-110 µmol/L)
<b>Urea</b>	8.1 mmol/L	(2.5-7.5 mmol/L)
<b>Adjusted calcium</b>	2.22 mmol/L	(2.2-2.6 mmol/L)
<b>ALT</b>	55 U/L	(7-55 U/L)
<b>ALP</b>	45 U/L	(45-115 U/L)
<b>Bili</b>	9µ mol/L	(<22 µmol/L)
<b>Albumin</b>	32 g/L	(35-55 g/L)
<b>HB</b>	104 g/L	(115-140 g/L)
<b>WBC</b>	$5 \times 10^9/L$	$(4-11 \times 10^9/L)$
<b>MCV</b>	90 fl	(80-96 fl)
<b>Platelets</b>	$170 \times 10^9/L$	$(150-400 \times 10^9/L)$
<b>Neut</b>	$2.0 \times 10^9/L$	$(1.8-8 \times 10^9/L)$
<b>CRP</b>	6 g/L	(<5 g/L)

Which is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	B12 and folate deficiency
<input type="radio"/>	Brain metastases
<input type="radio"/>	Paraneoplastic syndrome
<input type="radio"/>	Peripheral neuropathy related to chemotherapy
<input type="radio"/>	Spinal cord compression
<input checked="" type="radio"/>	Peripheral neuropathy related to chemotherapy <b>Correct</b>

ABVD is the first line chemotherapy regime in Hodgkin's lymphoma. It is a combination of Adriamycin, Bleomycin, Vincristine, and Dacarbazine.

Vincristine prevents the protein tubular from binding to chromosomes and separating them during the M phase of the cell cycle. One of the most common side effects of vincristine is peripheral neuropathy, which typically improves on cessation of the drug but some patients will be left with permanent symptoms.

B12 and folate deficiency is a possibility with this neuropathic distribution but is less likely given the normal MCV.

Spinal cord compression would not usually cause symptoms in this distribution. It classically presents with pain, followed by leg weakness and bowel and/or bladder dysfunction in the later stages.

Paraneoplastic peripheral neuropathy is possible in Hodgkin's lymphoma, but is less common than vincristine toxicity.

Hodgkin's lymphoma can result in brain involvement but this would not classically present with symptoms in this distribution.

### Question 201 of 206

Interferon alpha immunotherapy is used as a treatment for which of the following conditions?

(Please select 1 option)

<input type="radio"/>	Acute lymphoblastic leukaemia
<input type="radio"/>	Acute myeloid leukaemia
<input type="radio"/>	Burkitt's lymphoma
<input type="radio"/>	Hairy cell leukaemia
<input type="radio"/>	Myelodysplastic syndrome
<input checked="" type="radio"/>	Hairy cell leukaemia <b>This is the correct answer</b>

Interferon-alpha is an immune system hormone which is very helpful to a relatively small number of patients, and somewhat helpful to most patients. Most commonly, the drug helps stabilise the disease or produce a slow, minor improvement.

Alpha interferon at 2 million U/m<sup>2</sup> subcutaneously three times a week for 12-18 months can be used to salvage relapsed or refractory hairy cell leukaemia.

**Reference:**

### Question 202 of 206

Which one of the following is true of IgE?

(Please select 1 option)

<input type="radio"/>	Crosses the normal placenta
<input type="radio"/>	Is increased acutely in an asthmatic attack
<input type="radio"/>	Is increased in the serum of atopic individuals
<input type="radio"/>	Is involved in type 2 hypersensitivity
<input type="radio"/>	Is present in plasma in the same concentration as IgG

<input checked="" type="radio"/>	Is increased in the serum of atopic individuals <b>This is the correct answer</b>
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IgG is the predominant form of immunoglobulin in plasma at a concentration around 10,000 times that of IgE.

IgG crosses the placenta to confer immunity to the fetus but IgE does not.

IgE is involved in arming mast cells and basophils. IgE causes mast cells to release vasoactive amines, such as histamine, producing an inflammatory response which can result in a type I hypersensitivity reaction.

IgE is responsible for allergen-mediated diseases such as anaphylaxis, asthma, and atopy.

Total serum IgE is frequently increased in those with atopy but serum IgE does not rise acutely during an asthmatic attack.

### Question 203 of 206

A 54-year-old man comes to the endocrine clinic for review.

He has a history of type 2 diabetes which is currently managed with gliclazide 80 mg BD.

Most recently he has been diagnosed with abnormal liver function which the GP suspects is cirrhosis, although he claims he does not drink more than three to four glasses of wine per week.

He has split from his partner and admits to erectile dysfunction problems going back over the past three years.

On examination, he looks tanned and has signs of chronic liver disease. There is sparse secondary sexual hair.

Investigations show:

<b>Haemoglobin</b>	148 g/L	(135-180)
<b>White cell count</b>	$6.0 \times 10^9/\text{L}$	(4-10)
<b>Platelets</b>	$222 \times 10^9/\text{L}$	(150-400)
<b>Sodium</b>	139 mmol/L	(134-143)
<b>Potassium</b>	4.7 mmol/L	(3.5-5)
<b>Creatinine</b>	130 $\mu\text{mol/L}$	(60-120)
<b>ALT</b>	230 U/L	(5-40)
<b>Glucose</b>	10.5 mmol/L	(<6.0)

Which of the following is the most appropriate single test with respect to revealing the underlying diagnosis?

(Please select 1 option)

<input type="radio"/>	Hepatitis serology
<input type="radio"/>	Serum ferritin

<input type="radio"/>	Serum iron
<input type="radio"/>	Serum testosterone
<input type="radio"/>	Transferrin saturation

<input checked="" type="radio"/>	Transferrin saturation <b>This is the correct answer</b>
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The clinical presentation here is highly suspicious for genetic haemochromatosis. The best way to measure iron overload is via transferrin saturation which is calculated from the serum iron and the serum total iron binding capacity.

If the saturation is greater than 55% then genetic testing for the two commonest mutations, C282Y and H63D should be considered. Liver biopsy is indicated where there is evidence of liver damage, as indicated here by the raised alanine aminotransferase (ALT).

Treatment is with venesection, which is indicated until transferrin saturation falls to below 16%. Diabetes mellitus and hypogonadism may respond in some patients to venesection.

### Question 204 of 206

Which of the following is true for a patient whose pre-transfusion blood type is group O?

(Please select 1 option)

<input checked="" type="radio"/>	The red cells have A/B antigen but no antibodies in the plasma
<input type="radio"/>	The red cells have absent A/B antigen and plasma has anti-A and anti-B antibodies
<input type="radio"/>	The red cells have antigen A and plasma has anti-B antibodies
<input type="radio"/>	The red cells have antigen B and plasma has A antibodies

<input type="radio"/>	The red cells may have any antigen but plasma has anti-A and anti-B antibodies
<input checked="" type="radio"/>	The red cells have absent A/B antigen and plasma has anti-A and anti-B antibodies <b>This is the correct answer</b>

The answer options represent the following blood groups:

- Blood Group O - The red cells have absent A/B antigen and plasma has anti-A and anti-B antibodies
- Blood Group AB - The red cells have A /B antigen but no antibodies in the plasma
- Blood Group A - The red cells have antigen A and plasma has anti-B antibodies
- Blood Group B - The red cells have antigen B and plasma has A antibodies

The remaining incorrect answer option does not represent any blood group.

### Question 205 of 206

A 45-year-old woman being treated for acute myeloid leukaemia fails to get sufficient rises with platelet transfusions.

She is 14 days post-chemotherapy, afebrile and apart from minor bruising is otherwise well.

Which of the following would be the next best step in the management of platelet refractoriness?

(Please select 1 option)

<input type="radio"/>	Avoid further platelet transfusions
<input type="radio"/>	Check for a one hour post platelet transfusion platelet count
<input type="radio"/>	Continue to monitor for platelet rises with random platelets
<input type="radio"/>	Prescribe HLA matched platelets
<input type="radio"/>	Request directed platelet donations



Check for a one hour post platelet transfusion platelet count **This is the correct answer**

Patients who are refractory to platelet transfusions should first be investigated to check for adequate platelet rises. This is best done on a one or two-hour post platelet transfusion sample.

Further management would include checking for HLA antibodies but requesting HLA matched platelets at this stage would not be appropriate.

Continuing random platelet transfusions or requesting a directed platelet donation are also not appropriate at this stage.

Platelets are obviously indicated in this patient until recovery of blood counts and hence cannot be avoided.

#### Question 206 of 206

Mr YB is a patient who regularly attends the anticoagulant clinic.

He is very concerned as he has been recently started on a new drug by his GP. He asks you whether it would enhance the anticoagulant effect.

Which of the following may increase the potential for bleeding in patients taking warfarin?

(Please select 1 option)



Carbamazepine



Clopidogrel



Griseofulvin



Phenobarbitone



St. John's wort



Clopidogrel **This is the correct answer**

Clopidogrel does not appear to have a clinically relevant effect on the pharmacokinetics or pharmacodynamics of warfarin.

However, the concurrent use of clopidogrel with warfarin increases the bleeding risk.

All other drugs in the options are C-P450 enzyme inducers so would *decrease* the anticoagulant effect